Evaluation and follow up Of surgically managed Patients of Non Neurogenic Neurogenic Bladder

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CERTIFICATE

This is to certify that the dissertation entitled "**Evaluation and Follow up of Surgically Managed Patients of Non Neurogenic Neurogenic Bladder"** is the bonafide original work of **Dr Arindam Dastidar** submitted in partial fulfillment of the rules and regulation for the MCh Branch-V (Paediatric Surgery), examination of the Dr MGR Medical University, Chennai Tamil Nadu to be held in August 2009.

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INTRODUCTION

Voiding dysfunctions are one of the most frequently seen clinical entities in Paediatric urology. Traditional belief that it is only a learned behavior related to toilet training gone awry and resolves spontaneously if left alone is, incorrect (10).

It represents a spectrum ranging from benign incontinence to severe form like non Neurogenic Neurogenic bladder (Hinman's Syndrome).

What is understood is that it is an aberration in the normal development of lower urinary tract maturation and coordination. But why some patients have transient benign form of the disorder and others have chronicity and damaged upper tracts, is yet to be understood.

Anticholinergic medication and behavioral modifications has been the cornerstone of managing these patients. Patients presenting late or with severe upper tract changes including major VUR require surgical intervention. This may be temporary diversion (Ureterostomy), continent catheterisable channel (Mitrofanoff) or even augmentation Cystoplasty. Role of surgery has not been clearly defined in this subset of patient in the literature; aim is to break the dyssynergia to prevent further damage to upper tracts.

AIM

Evaluation and Follow up of Surgically Managed Patients of Non Neurogenic Neurogenic Bladder.

Review of literature

Relevant Anatomy and physiology

The Bladder is a unique organ in the human body which performs the function of storage and emptying of urine under a complex neural (voluntary and involuntary) control (19).

The Bladder wall consist of a meshwork of smooth muscle fibers arranged into a single functioning unit. The ability of the bladder to store urine (reservoir function) is determined by the concomitant activity of the detrusor muscle and the bladder outlet (consisting of bladder neck, posterior urethra, and striated muscle of the pelvic floor). The bladder sphincter (external and internal) plays a major role in urinary continence by closing the bladder neck and proximal urethra (19).

The External sphincter has an inner layer of smooth and an outer layer of striated muscle, extending from the apex of the prostate to invest the length of the membranous urethra in the male. In the female this is less well developed.

The internal sphincter however has not been well delineated anatomically. It has generally been accepted that it consist of smooth muscle fibers continuing from

the bladder base and trigone that traverse inferiorly through the bladder neck to extend towards the proximal urethra. Its existence has been better delineated in radiological and urethral pressure studies.

During the act of micturition the bladder base, bladder neck and proximal urethra can be

shown to contract simultaneously as a unit producing a funnel effect that opens up the bladder outlet with initiation of voiding.

Innervations:

Activation, coordination and integration of the various parts of bladder sphincter complex involve the central somatic and autonomic nervous systems, through three sets of peripheral nerves (19).

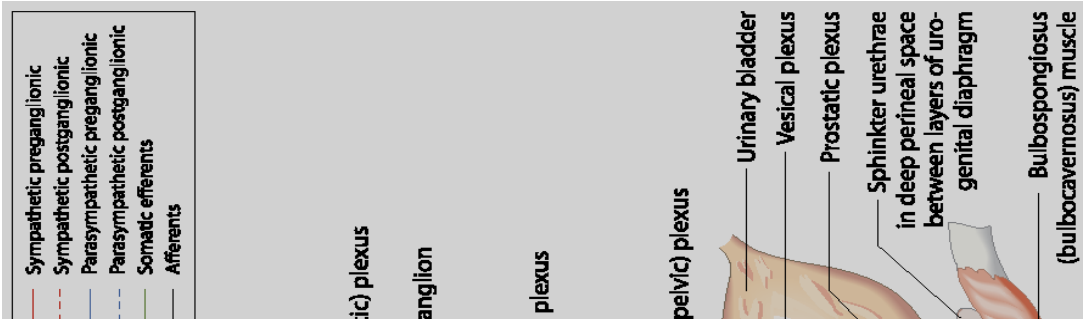
Sacral Parasympathetic (Pelvic nerve)

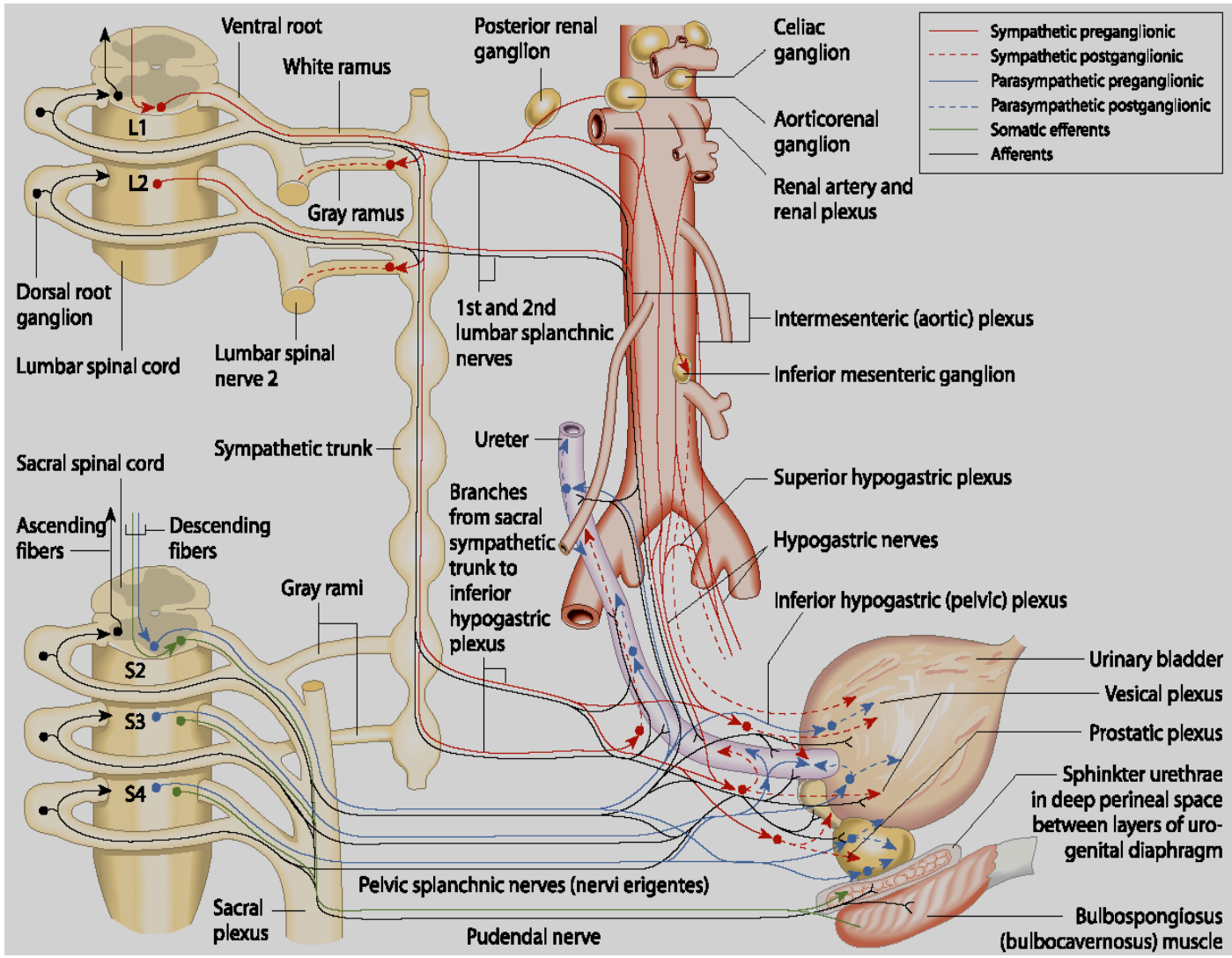
Thoraco-lumber sympathetic (Hypogastric nerve and Sympathetic chain)

Sacral somatic nerves (Pudendal Nerve)

During bladder filling, the viscoelastic properties of the bladder wall and an absence of an excitatory input from the parasympathetic ganglia to the bladder smooth wall musculature allow the bladder to accommodate more urine while keeping the pressure low (23). As bladder continues to fill an increase in outlet resistance occurs by means of a rhabdospinchter somatic reflex called the guarding reflex (20). In human and in many mammalian species, a sympathetic reflex also aids this process by increasing outlet resistance. This is achieved by increasing tension on the smooth muscle component of the sphincter and by inhibiting bladder contractility through an inhibitory effect on the

Innervations of Lower Urinary Tract




Ventral root
White ramus
Posterior renal ganglion
Celiac ganglion
Aorticorenal ganglion
Renal artery and renal plexus
Sympathetic preganglionic
Sympathetic postganglionic
Parasympathetic preganglionic
Parasympathetic postganglionic
Somatic efferents
Afferents
L1
L2
Gray ramus
Dorsal root ganglion
Lumbar spinal cord
Lumbar spinal nerve 2
1st and 2nd lumbar splanchnic nerves
Intermesenteric (aortic) plexus
Inferior mesenteric ganglion
Sympathetic trunk
Ureter
Sacral spinal cord
Ascending fibers
Descending fibers
Branches from sacral sympathetic trunk to inferior hypogastric plexus
Superior hypogastric plexus
Hypogastric nerves
Gray rami
Inferior hypogastric (pelvic) plexus
S2
S3
S4
Urinary bladder
Vesical plexus
Prostatic plexus
Sphinkter urethrae in deep perineal space between layers of uro-genital diaphragm
Pelvic splanchnic nerves (nervi erigentes)
Sacral plexus
Pudendal nerve
Bulbospongiosus (bulbocavernosus) muscle

parasympathetic ganglia. Finally the sympathetic output also decreases the tension of bladder smooth muscle.

Bladder emptying can be volitional or involuntary and involves an inhibition of the spinal somatic and sympathetic reflexes and activation of the parasympathetic pathways leading to the bladder. The coordination centre lies in the pons region of the brainstem (23).

Development of bladder control- plasticity, maturation and re-emergence

The neonatal bladder is not an effective storage organ (23). Bladder emptying in the neonate is classically thought to occur as a result of a sacral spinal cord reflex

In modern urodynamic parlance a new born through infancy and early toddler years has bladder instability. These early pathways become incorporated into more mature pathways by active inhibition from increasing cerebral maturation. Inhibition rather than cessation of these infantile reflexes is the important observation.

In newborn rat model, a primitive reflex the extroceptive perineal-to-bladder reflex is the principal voiding reflex until the mature spinobulbar or pontine micturition centre (PMC) based reflex begins functioning at several weeks of life (23).

Studies using pseudorabies virus tracing, cellular labeling, and CNS transaction preparation in animals demonstrate that, at newborn stage the bulbo spinal pathways that connect to the PMC are fewer and weaker. But as the neonate matures, there is pruning of interneurons to preganglionic synapses from afferent and increased synapses from the bulbospinal pathways. This synaptic plasticity and rearrangement

leads to maturation of voiding mechanism. Plasticity is not a one way process. Where

inhibitory control can be overlaid, they can also be removed. Disease process can decrease or eliminate inhibitory influences there by unmasking the primitive neonatal reflex. Literature suggests that immature detrusor-sphincter coordination, manifested as detrusor hypercontractility and interrupted voiding, commonly occurs in the first 1 to 2 years of life causing some degree of functional bladder outflow obstruction. In a postmortem study of the ontogeny of the external urinary sphincter in human fetuses, infants, and young children, Kokoua and colleagues (1992) found significant age-related differences in the histologic structure of the sphincter as compared with that in adults. Striated muscle fibers of the sphincter first appeared at around 20 weeks of gestation, then became arranged in a concentric pattern as a closed ring, fused posteriorly to form a tail-like structure that was directed to the perineal body. Posterior splitting of the striated sphincter, starting first caudally and progressively in a cephalad manner then occurred during the first year of life, coinciding in parallel with gradual resorption of the “tail,” to eventually giving way to a mature omega-shaped structure (19). Because a complete closed ring of striated sphincteric muscle was present up to 1 year of age in over 40% of cases, it may well be conjectured that this could be related to the high intravesical pressures and interrupted voiding that are commonly observed during urodynamic studies in infants

Voiding Dysfunction

Background, Terminology and Definition

Voiding pattern and acquisition of bladder control in healthy children are age and maturation dependent. A normal voiding cycle requires a bladder that expands easily during filling phase. Coordination between the bladder and external sphincter during this cycle evolves with age

and training.

Voiding dysfunction (dysfunction in this context excludes organic etiology) is caused by abnormality in one or both phases of the micturition cycle. Voiding disorder in the neurologically intact children is still not completely understood, but usually represents a medically benign although socially detrimental condition.

This is documented in 12-25 % of the children in the literature.

Definition

Dysfunctional voiding, defined as incontinence due to bladder sphincter dys-coordination is, over simplification of a complex problem. It is misleading because it explains nothing about detrusor and urethral behavior during filling.

It is difficult to accept that the few minutes in 24 hrs that voiding occurs may cause the profound bladder effects, such as trabeculation and upper tract changes that are seen in severe cases (16). Koff stated that bladder decompensation with high end filling pressure rather than high voiding pressure occurs in this pathological condition.

Classification (22)

Dysfunctional Voiding Disorders

a. Minor Dysfunctional Disorder

   Extraordinary Daytime Urinary Frequency Syndrome

   Giggle Incontinence

   Stress Incontinence

Postvoid Dribbling

Nocturnal Enuresis

b. Moderate Dysfunctional Disorder

Dysfunctional Elimination Syndrome

Overactive Bladder

Lazy Bladder Syndrome

c. Major Dysfunctional Disorder

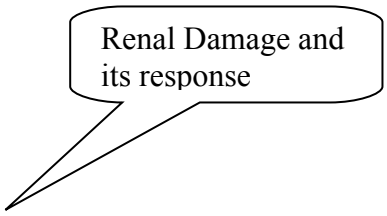
Transient Urodynamic Dysfunction of Infancy

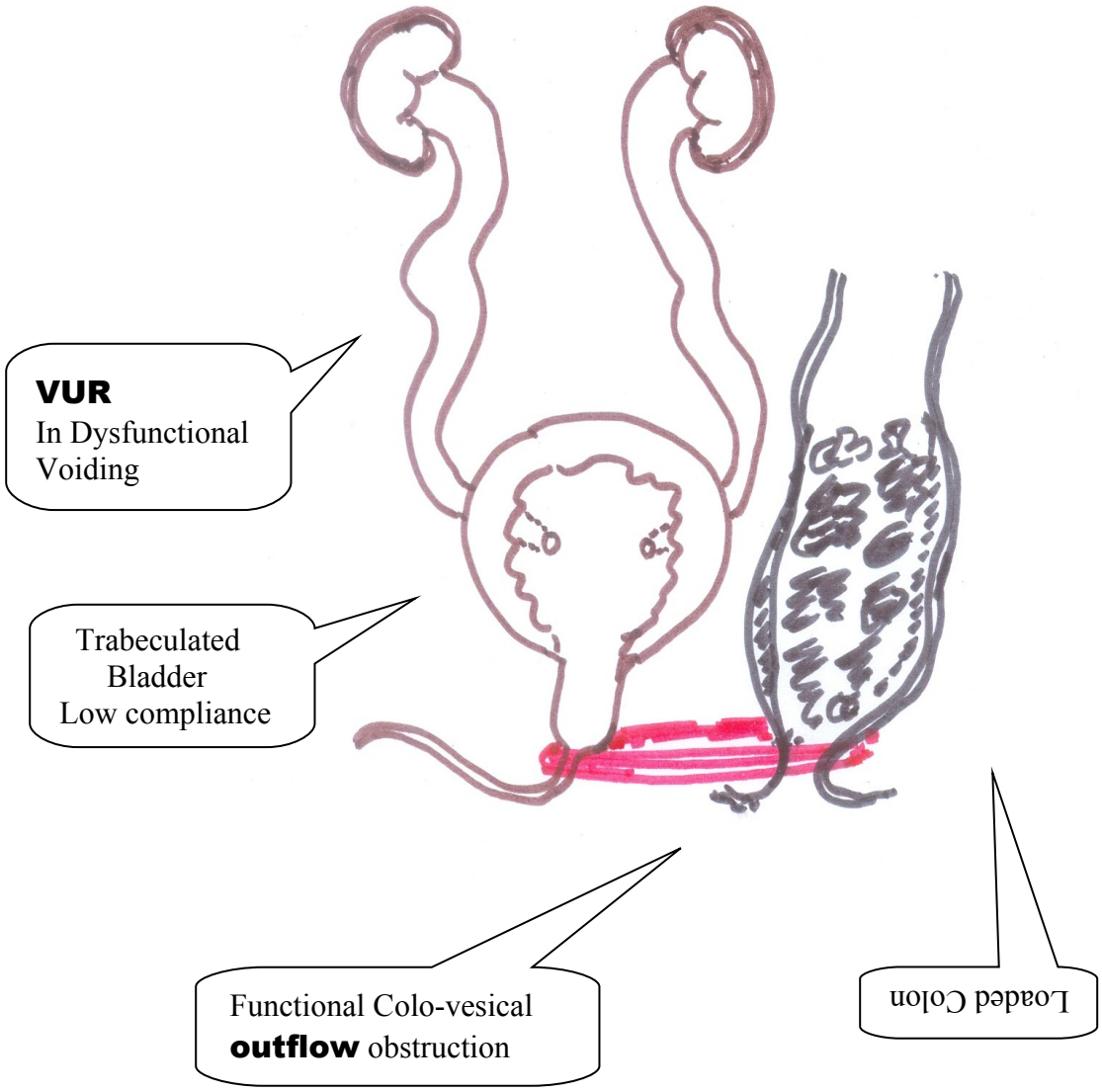
Hinman Syndrome (Non Neurogenic Neurogenic Bladder)

Ochoa Syndrome

Myogenic Detrusor Failure.

Factors involved in the Pathophysiology of a Severe Dysfunctional Voiding





Functional outflow obstruction

This distinguishes it from a fixed outflow obstruction like PUV, stricture. A functional outflow obstruction can be neurogenic or non neurogenic origin. Children with NNNB have an in coordination between the detrusor and its outflow (the external sphincter). This has been

suggested to be due to a delay in maturation of the bladder or a persistence of infantile bladder control. While an infantile bladder contraction initiates voding, an older child may perceive them as appearing under unacceptable condition. A voluntary contraction of external sphincter to prevent the bladder from emptying initiates a cycle of stasis, incontinence and eventually upper tract drainage.

Urodynamics (with perineal EMG) and Micturating cystourethrogram has helped in the understanding of this functional obstruction. The characteristic finding is of a dyssynergia between the detrusor contraction and external sphincter relaxation. On an MCU, the part of urethra proximal to the external sphincter (Posterior urethra) appears dilated during voiding phase (Spin Top Urethra). Unlike a non fulgurated valve this dilatation is transient and it may diminish or disappear at Cystoscopy or after successful biofeedback treatment. Fred Johnson et al postulated this posterior urethral dilatation to be an attempt to protect the upper tract from deteriorating (9).

Over active bladder

Detrusor overactivity is the most common voiding dysfunction in children (18). The prevailing theory is of a delay in acquisition of cortical inhibition over uninhibited detrusor contraction in the course of achieving the mature voiding pattern of adulthood. This results in delay of fine tuning bladder sphincter coordination. Which means an involuntary detrusor contraction meets a voluntary external sphincter contraction of which the control is thought to be acquired at an earlier age. This results in increased in increased intravesical pressure, further worsening the bladder overactivity.

The traditional belief that a child outgrows this incoordination has been disproved. Studies have shown association of neuro-psychiatric, sexual dysfunction in adults to presence of neglected OAB in childhood (5, 18). Progress of a simple untreated OAB to severe form of

dysfunctional voiding is well documented. Treatment is individualized keeping in mind the severity of presentation

LUTS and VUR

Bladder dynamics have major role in the normal functioning of ureterovesical junction. Anatomically an UV junction evolves gradually with the growth of the child. This evolution passes through a phase during which bladder is learning to store and empty effectively. In other words, during this period there is a short length of tunnel and a high intravesical pressure, factors which promote vesicouretric reflux.

The reported prevalence of bladder dysfunction with VUR varies depending on the mode of diagnosis. Where invasive urodynamic investigation were used, higher figure were noted(38-75%) in contrast to when non urodynamic investigation were used(18-52%) (7).
It is important to view reflux as an outcome of mechanical and dynamic disturbance of the uretero-trigonal unit. In majority of the patient this occurs in combination of varying proportion. To understand the relation of bladder dysfunction and reflux one must understand that dysfunctional bladder is a broad terminology, which includes OAB at one end Dysfunctional voiding at the other. Although in a given patient both this entity may coexist, it's important to differentiate the predominant character of the dysfunction before treatment is initiated. The concept of dysfunctional elimination syndrome (DES) was introduced by Koff et al. he reported it to be present in 46% of children with primary reflux. He found that both the rate of UTI (Scarring) and spontaneous resolution of vur were adversely influenced by the presence of DES.

Treatment of bladder dysfunction depends on the identification of predominant type. OAB responds to anticholinergics whereas dysfunctional voiding requires a combination of anticholinergics, alpha-blockers, CIC or biofeedback. The results of treatment with respect to VUR resolution are conflicting in the literature. Older studies (Koff) has shown an increased resolution compared to newer one (Willemson and Nijman)(Snodgrass). Reimplantation of a refluxing ureter in an unstable bladder carries a high risk of failure unless measures are taken to treat the bladder pathology.

Can reflux precipitate bladder dysfunction? From the available studies it is difficult to answer that. But if this disorder is visualized as an embryological anomaly of uretric bud and trigonal development; it can explain the close association of the two disorders (7). In a subset of patient, bladder dynamics may actually improve after endoscopic injection treatment (7) because, large refluxing urine volume can induce extra volume load on the detrusor, stimulating a voluntary contraction of the pelvic muscle. Over time this results in stasis, trabeculation and progressive renal scarring.

Bladder compliance

Bladder compliance describes the relation between change in bladder volume and change in detrusor pressure. Compliance is calculated urodynamically by dividing the (ΔV) by the change in detrusor pressure (Δdet) during that change in bladder volume. It is expressed in ml/cm.

For an effective emptying of ureter, bladder needs to be accommodative. This is influenced by stiffness of bladder wall and nature of outlet. Low compliance, i.e stiff bladder may be due to

diverse conditions including myelodysplasia, multiple sclerosis, radiation induced detrusor injury or obstructive uropathy. The exact mechanism involved in the development of altered bladder compliance is currently unknown but the process is believed to be common to all condition. Bladder outlet obstruction results in alteration in bladder physiology, including wall thickening and

decreased capacity. This reduction of capacity and compliance is due to increase in smooth muscle cell component and excess matrix (collagen) deposition(3) . Presently its not known why this process results in a thick walled noncompliant bladder or a decompensated bladder and why compliance sometimes continues to decrease even after deobstruction.

When a child exhibit severe bladder outlet obstruction resulting from either an anatomic or a dyssynergic cause, progressive bladder dysfunction is likely to ensue. Effort to reduce intravesical pressure by either relieving the obstruction or periodically emptying the bladder by CIC will prevent progression to end stage bladder dysfunction and eventually end stage renal injury.

Although 40 cm of water is mentioned as cut off for potential renal damage, laboratory study involving human bladder smooth muscle cell has shown that pressure as low as 20 cm H_2O may lead to molecular changes consistence with decreased bladder tissue compliance (3).

The gold standard in the management of a low compliance bladder is CIC with anticholinergics. This not only prevents further decrease in compliance but also protect upper tract complication.

Bladder augmentation is reserved for heavily trabeculated bladder which are resistant to conservative measures.

Renal response to obstruction

Damage to the distal nephron due to increased intraluminal pressures causes impaired urine concentrating ability, polyuria and polydipsia (nephrogenic diabetes insipidus) which may or may not be associated with impaired
glomerular function (23). This increased urine output with an abnormal bladder worsens lower tract symptoms (incontinence) and promotes secondary renal damage. The normal response to a reduction in numbers of functioning nephrons, as in renal dysplasia, is to increase the amount of work done by individual nephrons (single nephron GFR) by a combination of nephron hypertrophy and hyperfiltration. The latter is a result of vasodilatation of the afferent arterioles leading to an increase in the glomerular plasma flow and glomerular capillary hypertension (23). There is a disproportionate increase in glomerular filtration rate as the fraction of afferent blood filtered is increased, hence the term hyperfiltration. In time proteinuria and hypertension develop, coinciding with glomerulosclerosis and decreasing GFR, ultimately resulting in renal failure.

CONSTIPATION AND BLADDER DYSFUNCTION

Children with dysfunctional voiding and recurrent UTIs often have associated bowel dysfunction, including constipation, fecal impaction, and encopresis (19). However, only recently has the term dysfunctional elimination syndrome been given to recognize the existence of this relationship. Studies have been performed to explain how constipation and chronic rectal dilatation may interfere with the normal function of the lower urinary tract, resulting in bladder dysfunction, reflux, and UTIs (19) .The close proximity of the rectum to the posterior wall of the bladder makes it possible that any gross distention of the rectum by impacted feces can result in mechanical compression of the bladder and bladder neck,

leading to urinary obstruction(19) .In addition, it has been observed that large fecal impaction may induce significant detrusor instability and other bladder dysfunctions, which in turn will result in the urge syndrome, UTI, and reflux (19).

Natural history

The natural evolution of dysfunctional voiding is regression in 15% of cases every year (11). Because of the risk of self esteem impairment and/or potential damage to the urinary tract, treatment is proposed.

Using a combination of modalities (anticholinergic, antibiotic prophylactic, biofeed back and psychological counseling) NA Saedi followed 98 children diagnosed with voiding dysfunction with a mean follow up time of 1.6 years showed that 91% of the patient with day time wetting are completely cured and are totally dry during the day. The mean time for resolution is 2.8 years. Night time wetting was seen in 82% of followed up patients. And of these patients 84% no longer have night time wetting. The mean time for the resolution of this problem was approximately 4 years (11).

The Nonneurogenic Neurogenic Bladder (Hinman's Syndrome)

The Nonneurogenic Neurogenic Bladder (NNNB) syndrome, starting from the term itself, describes a contradictory and apparently nebulous identity (21). In spite of urodynamic techniques refinements and reports on terminology availability there is a not clear definition of the syndrome. In terms of etiology, there is not a cut off distinction with the dysfunctional voiding on one site and with isolated (or occult) neurogenic disorders on the other site, the latter being just a matter of exclusion.

Since the first description by Hinman in 1970 of the classical case of a 8 year old boy cured by hypnosis , the concept that the consequences upon the bladder and upper urinary tract may be initiated by pure functional circumstances and do not depend on unrecognized neurogenic lesions, received widespread consent along three decades and remained unchanged. Now days it is widely accepted that the condition is the extreme end stage of dysfunctional voiding

Presentation

Typically, children present with urinary incontinence after a period of initial continence and recurrent urinary infection. In rare cases first symptom is an acute urinary retention and urosepsis in infants. constipation and soiling are common and psychological disturbances are often evident.

Age of presentation.

Overall dysfunctional voiding occurs between 3-7 years , rarely it has been reported in the first year of life and also beyond puberty

Congenital NNNB

Beer in 1915 & Jayanthi in 1997 reported infants with features of Major dysfunctional disorder, thus challenging the whole concept of dysfunctional voiding being an acquired disease (8).

EVALUATION OF NON-NEUROPATHIC BLADDER-SPHINCTER DYSFUNCTION

History

The majority of children with non-neuropathic bladder-sphincter dysfunction typically present after toilet training with symptoms of either night-time or day-time urinary incontinence or both. Occasionally they can be recognized at an earlier age when the child presents for investigation of UTIs or VUR. In any case, it is important to obtain a detailed history from the child and guardian. This should include relevant questions to exclude neurologic and congenital abnormalities. Bowel dysfunction can coexist in the form of encopresis, constipation, and fecal impaction and should be noted during history taking. The urinary history should focus on symptoms related to both the storage and evacuation of urine.

Voiding Diary

A voiding diary is used to record daily fluid intake and urine output at home under normal conditions. When properly filled in, it can be very informative and give clues to the underlying

dysfunction. The number of voidings per day, the distribution of voids during the day, and each voided volume is recorded. It can also record any episodes of urgency and leakage. It is a useful tool to help identify those who may warrant further studies as well as in follow-up of patients

Physical Examination

Physical examination is usually normal in children with non-neuropathic bladder-sphincter dysfunction, but careful examination is required to exclude those who may require further neurologic evaluation. Occasionally, in an otherwise normal child, one may find a palpable bladder on abdominal examination in cases of decompensated bladders. Abnormalities of the lower spine should be sought specifically to exclude the possibility of an occult spinal dysraphism. Lesions such as an asymmetrical gluteal fold, hairy patch, dermovascular malformation, or lipomatous abnormality of the sacral region should prompt further imaging evaluation. The external genitalia may be examined to exclude any obvious anatomical problems that can explain the urinary symptoms in question. Rectal examination may reveal fecal impaction or distended rectum in those with chronic constipation.

Laboratory Investigations

Laboratory investigations are directed to assess renal function and presence of bacteriuria. Serum and urine osmolality may be looked at in cases of nocturnal enuresis to assess renal concentrating ability.

Ultrasonography

Ultrasonography is often the first-line investigation in children with non-neuropathic bladder-sphincter dysfunction because it is a simple, readily available, and noninvasive tool that is able to provide information both on anatomic and functional problems when performed by experienced pediatric radiologists.

Ultrasonography has been increasingly used in the study of the pelvic floor musculature. In boys, the external sphincter, puborectalis, and bulbocavernosus have been observed to contract during a hold maneuver. In girls, lengthening of the urethra and movement of the bladder neck in the direction of the symphysis is seen. However, in patients with nonneuropathic bladder-sphincter dysfunction, approximately one third of the children were unable to elicit movement of the pelvic floor or had paradoxical movement The clinical significance of this remains unclear, but when introduced to a period of urotherapy and pelvic floor rehabilitation, marked improvement of symptoms had been reported. Similarly, ultrasonography has been employed in the study of bladder neck mobility. Studies have shown that in a proportion of girls with hyperlaxity of joints, coughing or straining would result in a wide opening of the bladder neck and urethra. In this group of girls, urotherapy would prove difficult and occasionally some would go on

to require surgery to the bladder neck (de Jong, 2005). Ultrasound can provide a noninvasive means to monitor this subgroup of children not responsive to standard urotherapy. More recently, ultrasound has been used to measure bladder parameters used in calculating a *bladder volume and wall thickness index* (BVWI). This BVWI can be classified into normal, thick, or thin according to the measured parameters. Our studies have shown that these classifications corresponded closely to urodynamic findings of underlying bladder dysfunctions and can act as a reliable tool to guide for further invasive investigations (Yeung

et al, 2004).

Other Imaging Studies

Radiologic examination of the spine may be necessary to rule out any neurogenic causes of bladder-sphincter dysfunction.

A micturating cystourethrogram may be performed in patients to rule out VUR. Information on the bladder emptying efficiency may be obtained and the status of the urethra can be assessed to exclude any outflow obstruction.

Role of MRI in the management of NNNB

The diagnosis of NNNB is made by exclusion based on a constellation of clinical, radiographic and/or urodynamic findings. Typically there is evidence of severe abnormal bladder function that mimics the effects of outflow obstruction or underlying neuropathy. If neither of these two conditions is present, one may use the term Non Neurogenic Neurogenic Bladder. A Neurogenic lesion can be obvious or occult. The dilemma in evaluating an incontinent child with no obvious neurogenic lesion is the role of a routinely MRI. There are contrasting reports in the literature regarding its role.

Pippe Salle in their study of patients with normal neuro-orthopedic examination and dysfunctional elimination syndrome reported that MRI should be used in patients with abnormal physical findings or complex abnormality on spinal x-ray.

KAfshar et al (13) noted that spinal MRI has a low impact on the management of LUTS. With proper case selection the pre test probability of positive MRI may be increased and therefore many unnecessary studies may be avoided.

In contrast Douglas A Canning in an editorial comment (25) and E Wraige believe spinal cord

imaging by MRI should be considered in children with incontinence when this is associated with impaired bladder sensation or poor emptying even in absence of neuro-orthopedic, cutaneous or lumbosacral spine x-ray abnormalities. They believe a detrusor instability may be the earliest sign of an occult spinal lesion.

Luis et al (24) noted after untethering day time incontinence improved dramatically, this was confirmed urodynamically as well. But they also commented on lack of proven indication and long term follow up data of surgical intervention in occult spinal dysraphism.

We have been selective in the use of spinal MRI in our patients. The yield is poor in absence of cutaneous and neuro-orthopedic abnormality. It is expensive and requires General Anaesthesia in young children. Our protocol is to evaluate the child with a thorough neuro-physical examination and a LS spine x-ray. MRI is done if there are LS cutaneous stigmata, abnormal LS X-ray (other than spina bifida Occulta) or a neuro-orthopediac deformity/anorectal malformation. Such cases have been excluded from this study.

Urodynamic Studies

The classical urodynamic pattern of NNNB is sphincter hyperactivity and overactive detrusor at voiding(Dyssynergia), which can be associated with overactivity with unstable detrusor during filling.

All urodynamics should be preceded by or combined with a uroflow study. When performing uroflowmetry, the child must experience normal desire to void for it to be representative and repeated recordings should be performed. Preferably, the voiding should be observed and correct sitting or standing position ascertained.

MANAGEMENT OF NON-NEUROPATHIC BLADDER-SPHINCTER DYSFUNCTION

Behavior Modification and Standard Urotherapy

Urotherapy is a nonpharmacologic and nonsurgical combination of cognitive, behavioral, and physical therapy with an aim to normalize micturition pattern and prevent further functional disturbances of the lower urinary tract The children and their parents are educated on proper voiding mechanics, and the specific problem is explained to them to provide motivation for improvement. Specific instructions are then given as to how and when to void. Children are assessed and taught correct sitting or standing positions for voiding. They are taught how to relax the pelvic floor and avoid straining. Their drinking and voiding habits are studied and modified accordingly to include proper hydration with timed voiding.

A proper assessment of their bowel function is imperative to successful management. To achieve good results, strong patient support with adequate motivation of both the child and the parents are essential.

Biofeedback and Pelvic Floor Rehabilitation

Biofeedback is based on the concept of building selfperception on detrusor contractions and pelvic floor relaxation in the patient By combining uroflowmetry with real-time monitoring, the child is able to see how well he or she is voiding. It also helps the child understand what can be altered with voluntary control and with relaxation of the pelvic floor. Biofeedback as a treatment modality for children with dysfunctional voiding is

based on this concept and has proven to be highly effective either on its own or in

combination with standard urotherapy

Neuromodulation, Acupuncture, and Other Treatment Modalities

Recent studies reported that transcutaneous electrical nerve stimulation (TENS) is a simple, cost-effective, noninvasive treatment modality for the management of a wide variety of lower urinary tract disorders with few side effects (19). The mechanisms of action of the reported techniques remain unclear, but symptomatic improvements are common. Some reports indicate changes in urodynamic parameters during transcutaneous stimulation, suggesting that the TENS therapy was capable of inhibiting detrusor contractions. The beneficial effects of TENS over the sacral dermatomes (S2-S3) in patients with lower urinary tract symptoms associated with detrusor overactivity have been reported. The use of low frequency electrical current to inhibit detrusor activity in adults is common and appears to modulate excitatory and inhibitory components of bladder control Such studies provide the rationale for the application of TENS therapy to modulate detrusor function in patients with functional detrusor dysfunction.

Traditional acupuncture has also reported high efficacy in the treatment of nocturnal enuresis with low relapse rate. Reports have used acupoints innervated by sacral segments S2-S4, and stimulation involved both manual and electrical stimulation. However, its use in the pediatric population remains limited by the intrinsic fear of needling in children with subsequent lack of cooperation (Bower et al, 2005).

Bowel Management (19)

The principles of bowel management include rectal emptying of impacted stool and the maintenance of regular soft stools A reliable bowel habit pattern can only be established

when the child is able to achieve pain-free defecation of soft stool. An initial cleanout of the bowel can be achieved by oral laxatives and rectal enemas on a regular basis until complete disimpaction of the rectum. Occasionally, high colonic washouts may be necessary to achieve a good result. Only when this has been achieved should the second stage of management commence, which involves prevention of further stool accumulation with continuation of regular oral laxatives and/or stool softeners as well as dietary modification. Correct toileting posture and correct recruitment of abdominal muscles in the defecation process aids in the effectiveness of bowel emptying. However, success of a bowel management program can only be achieved with sound support from the family. Parental education is necessary so that the parents can help reinforce and encourage correct toileting habits at home.

Medications

Pharmacologic control of the lower urinary tract can either act via the CNS or peripherally. Several CNS regions have been identified to be involved with micturition control, including the cortex, pontine tegmentum, medulla, and spinal structures. All these regions are modulated by several different neurotransmitters, which have become targets for drug treatment. However, many of the drugs developed with CNS action are not sufficiently selective to effect only the lower urinary tract, hence the possibility of

these drugs causing adverse drug reactions Pharmacologic targets for treating bladder dysfunction may be aimed at the bladder, urethra, ganglia, or peripheral nerves. The main targets for drug therapy are receptors or ion channels known to be involved in bladder contraction (e.g., muscarinic receptors, L-type calcium channels). More recently, research has been focused more on alternative neurotransmission and modulation of afferent signaling from the lower urinary tract.

Antimuscarinic Agents

These agents are the gold standard in treatment of overactive bladders(19). Muscarinic receptors are found in the human detrusor muscle, and bladder contractions are initiated by stimulation of these receptors with the release of acetylcholine from cholinergic nerves. The main action of antimuscarinics is on the M1 and M3 receptor subtypes, which are thought to be responsible for the pathogenesis of detrusor overactivity. Antimuscarinics, such as oxybutynin, act by reducing the frequency and intensity of involuntary contractions, resulting in an increase in the functional bladder capacity The clinical efficacy depends on various factors, such as receptor affinity, pharmacokinetics, and the specificity for the bladder. Latest developments have focused on receptor specificity and the ratio of efficacy to side effects. The nonselective pattern of activity and penetration of the blood-brain barrier are known to induce systemic and central side effects

α-Adrenergic Blockers

The body of the bladder receives relatively sparse innervation by noradrenergic nerves. The density of noradrenergic nerves increases markedly toward the bladder neck, where the smooth muscle receives a dense noradrenergic nerve supply, particularly in males. The normal response to norepinephrine is relaxation of the detrusor and contraction of the bladder neck. α-Adrenergic blockers are therefore used in patients with evidence of bladder neck dysfunction for relaxation of the bladder neck

Other Medications(19)

Tricyclic antidepressants such as imipramine have been found to be effective for increasing urine storage by both decreasing the detrusor contractility and increasing outlet resistance. However, the precise mechanism of action is not well explained. Their possible effect on the bladder outlet has been described by inhibition of norepinephrine reuptake producingα-adrenergic stimulation. These agents are associated with a high incidence of side effects, and their use should be judicious.

β-Adrenergic agonists can cause significant increases in bladder capacity but can also cause significant cardiovascular side effects.

Parasympathicomimetics, calcium antagonists, potassium channel openers, and prostaglandin inhibitors have all been described for use with effect on the bladder, but these are rarely used in children, either owing to their unfavorable side effects or to a lack of proven efficacy.

Clean Intermittent Catheterization

Clean intermittent catheterization may become necessary in children with decompensated bladders or lazy bladder syndrome where bladder emptying efficiency is compromised and upper urinary tract dilatation may exist. Regular emptying of the bladder to achieve low-pressure emptying improves detrusor contractility and bladder emptying function. Therefore, a regular clean intermittent catheterization program can allow for bladder retraining. Some of these children may be able to eventually be weaned from use of this procedure(19).

Surgery

When conservative management with nonpharmacologic and pharmacologic treatment fails,

surgical approaches may need to be considered. Bladder augmentation may be performed to help produce a low-pressure system with increased bladder capacity Augmentation may be performed using intestinal segments such as colon, ileum, or stomach. However, the complications that may ensue must be considered, including mucus production, electrolyte imbalance, and even possible metaplasia/malignancy.

Surgical means have also been employed to reduce urethral/sphincteric pressure as an alternative to α-adrenergic blockers.

Management of reflux

Mechanism of reflux in a setting of voiding dysfunction is high intravesical pressure which over a period of time results in distortion of VU junction. In a non dilating reflux with adequate size bladder a simple reimplant and a channel for CIC (Mitrofanoff) will be sufficient. Where as a heavily trabeculated bladder with dilating reflux will require an augmentation with some antireflux measures (reimplantation, TUU).

Recent studies have focused on the use of balloon dilatation of the bladder neck and botulinum A toxin injection into the urethral urinary sphincter in children with non-neuropathic bladder-sphincter dysfunction with very promising results. However, these methods seem to require repeated attempts and the long-term effect and efficacy have yet to be presented.

Materials and Methods

Patient Selection

Inclusion Criteria

- All surgically managed patients presenting with Lower Urinary Tract Symptoms (LUTS) with radiologically demonstrable bladder and upper urinary tract changes and without congenital structural anomalies in the urinary, neurological, anorectal systems or syndromic condition .

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Exclusion Criteria

Patient who had lower urinary tract symptoms but had evidence of

- Structural outlet obstruction (Posterior urethral Valve).
- Clinically demonstrable neurological lesion other than bladder or bowel symptoms.
- Cases of anorectal malformation.
- Any syndromic disease like Down's Syndromes, Prune Belly Syndrome

Spina Bifida Occulta without clinical evidence of tethered cord was included in the study. MRI was not done as a routine

Henceforth these patients will be termed as having

"Non Neurogenic Neurogenic Bladder"

Study Design

This is a descriptive study with both retrospective and prospective component. The operative records and follow up data were collected from the hospital charts. Follow up was conducted in the outpatient department.

Patient unable to travel to the hospital were contacted over the telephone and instructed to do necessary investigation locally.

Archived radiological investigations were fetched online to compare with latest images during follow up.

Selected Patients and Management Protocol.

28 patients with radiologically demonstrable trabeculated bladder, dilated upper tracts with LUTS were selected based on the above inclusion and exclusion criteria.

They were evaluated with thorough history, clinical examination (including blood pressure and neurological examination), urine analysis, hemoglobin, Creatinine, serum electrolyte.

The Urinary tract was evaluated with ultrasonography (any PVR was noted), Micturating Cystourethrogram and Cystoscopy.

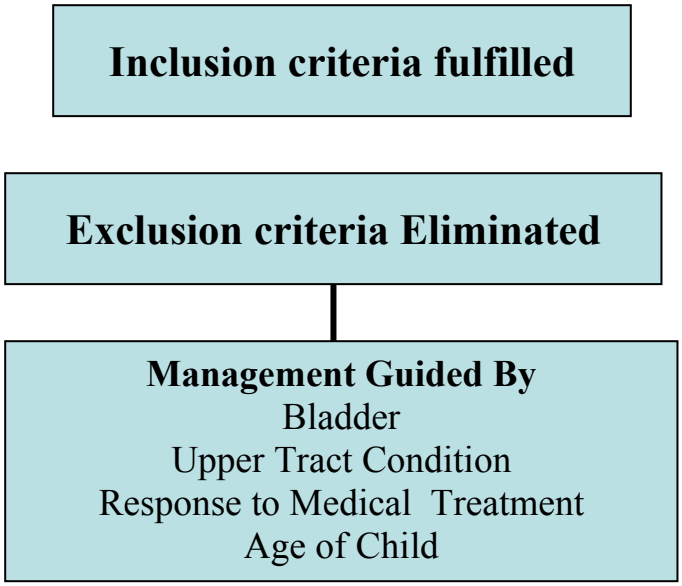
Spine was evaluated with lumbosacral plain X-ray. MRI was done selectively to rule out a tethered cord in children with cutaneous markers, abnormal lower limb power, tone, and reflex or any other neurological deficit outside the bladder. If tethered cord was detected, these cases were excluded. DMSA nuclear scan was done in patients with evidence of Vesicouretric reflux.

Urodynamic technique (N=10): Saline CMG was done to look for bladder sensation, detrusor contraction, compliance, leak point pressure and voiding pressure. Sphincter EMG

was not assessed as we did not have the facility.

Post cystometry, residual urine and upper tract changes were evaluated with ultrasound.

Management algorithm



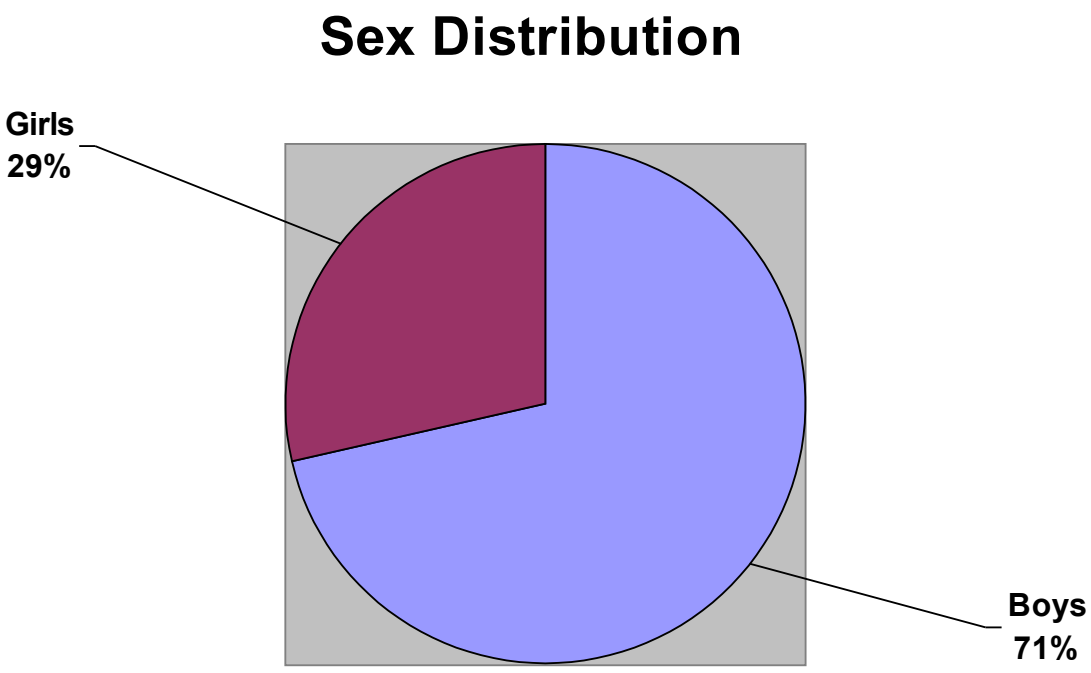
Age and Sex.

28 patients with non Neurogenic Neurogenic Bladder were operated between 1997 and 2008.

There were Boys: 20/28 (71%)

Girls: 08/28 (29%)

The youngest patient at presentation in this group was a 3 month old boy, while the eldest was a 14 year old boy, the average age was 5.17years (Girls 4 years, Boys 5.64 years).



Symptoms

All patients had lower urinary tract symptoms, which was defined as incontinence, frequency, urgency or obstructive symptoms (like retention in absence of anatomical cause) with or with out recurrent urinary tract infection.

Symptoms were documented according to ICCS recommendation and tabulated as storage or voiding symptoms.

Storage

Incontinence (Dribbling)	n = 19

Frequency	n = 01
Enuresis	n = 04

Voiding

Straining	n = 06
Retention	n = 07 ✶
Hesitancy	n = 01
Weak stream	n = 05

✶ Includes 5 catheter dependent patients.

Other symptoms

Recurrent Urinary Tract Infection/Fever/Dysuria	N=22
Constipation	N=6
Chronic indwelling catheter	N=5
Uremia	N=11
Hypertension	N=2

7 patients had history of surgical intervention prior to the recognition of ***Non Neurogenic Neurogenic Bladder***.

Previous surgical procedure

Diagnostic Cystoscopy	N= 2
Suprapubic cystostomy	N=1
Urethroplasty(For Hypospadias))	N=1
Unilateral reimplantation for suspected VUJ obstruction	N=2 units
TUU and reimplant for reflux.	N=1(2 units)
Temporary diversion (Ureterostomy)	N=2

Laboratory investigations

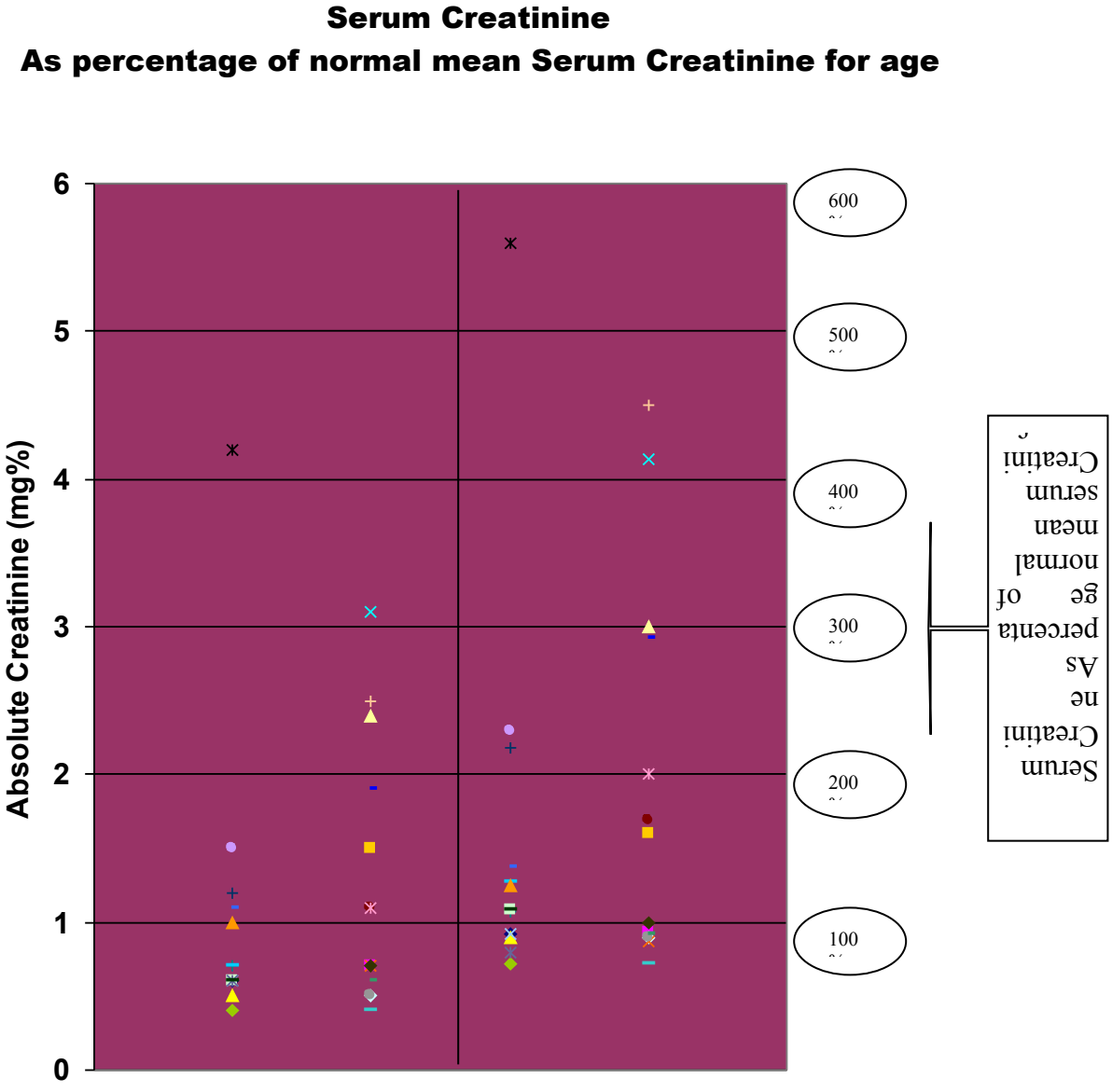
Urine microscopy, culture sensitivity, serum Creatinine and electrolytes were checked preoperatively as a routine. Patients presenting with uremia also underwent estimation of calcium, phosphorus, alkaline phosphatase. Preoperative serum Creatinine values were grouped into 3 levels.

Preoperative Serum Creatinine in 28 patients

Low ≤0.5 mg %	N=5
Medium 0.6-1 mg%	N=12
High ≥ 1.1 mg%	N=11

Preoperative serum Creatinine in the whole group had a mean of 1.1 mg% (range 0.4-4.2 mg %). Patients who presented in a state of uremia had an average Creatinine of 1.96mg%

(range 1.1-4.2mg %).



When Serum Creatinine was expressed as a percentage of the mean normal serum Creatinine for age, a more severe degree of renal failure was detected in 17 patients. The mean percentage was 224% (range 100-560%).

Radiology

Radiological evaluation was done using ultrasonography, Micturating cystourethrogram and spinal imaging.

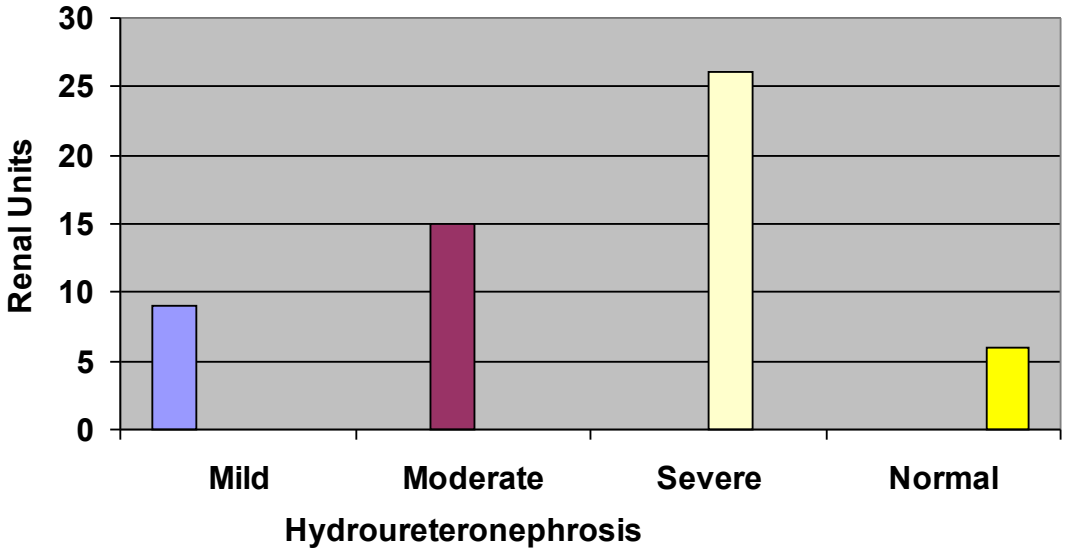
Ultrasonography.

56 renal units were analysed preoperatively, Hydroureteronephrosis was noted in 50 renal units.

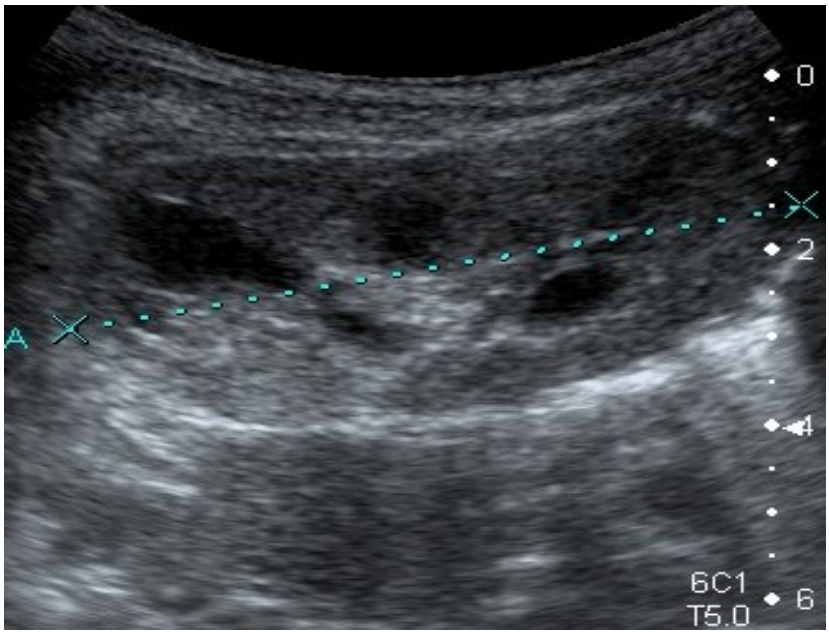
Unilateral hydroureteronephrosis	N=06 children
Bilateral hydroureteronephrosis	N=22 children
Total	N=28

Severity of Hydroureteronephrosis was grade into Mild, Moderate and Severe Renal Units.

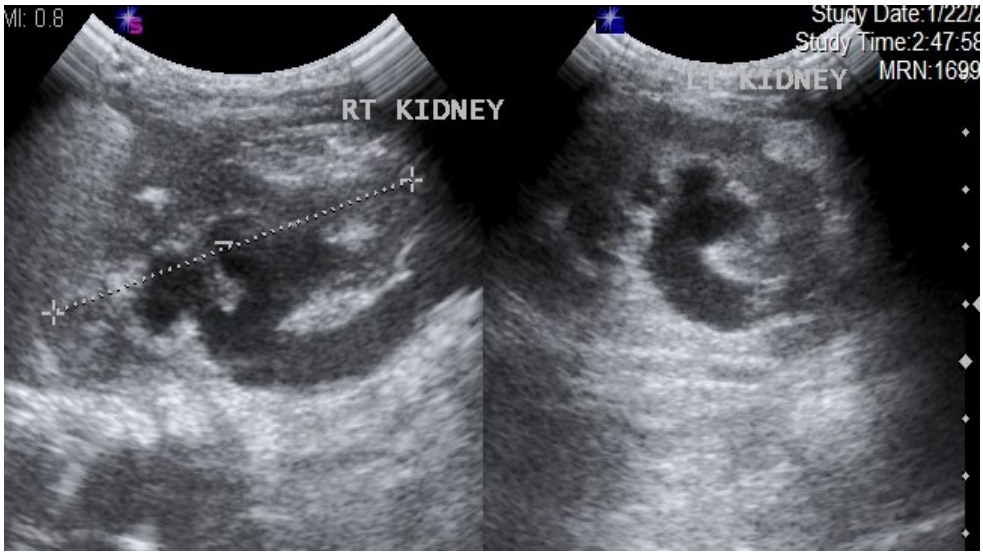
Severe Hydroureteronephrosis	N=26 Renal units
Moderate Hydroureteronephrosis	N=15 Renal units
Mild Hydroureteronephrosis	N=9 Renal
No Hydroureteronephrosis	N= 6 Renal units
Total	**N=56 Renal units.**



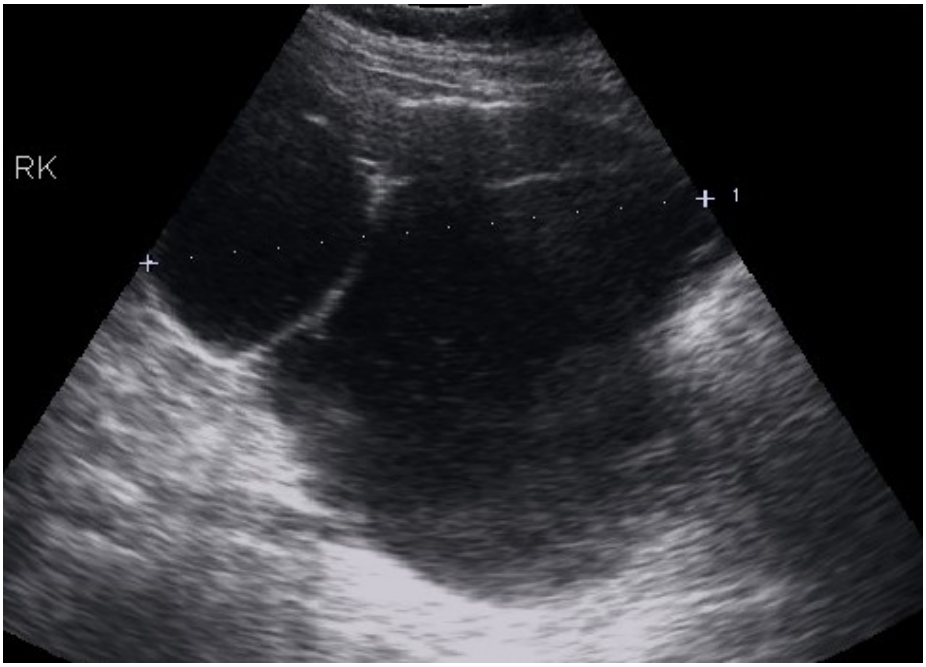
Mild Hydroureteronephrosis



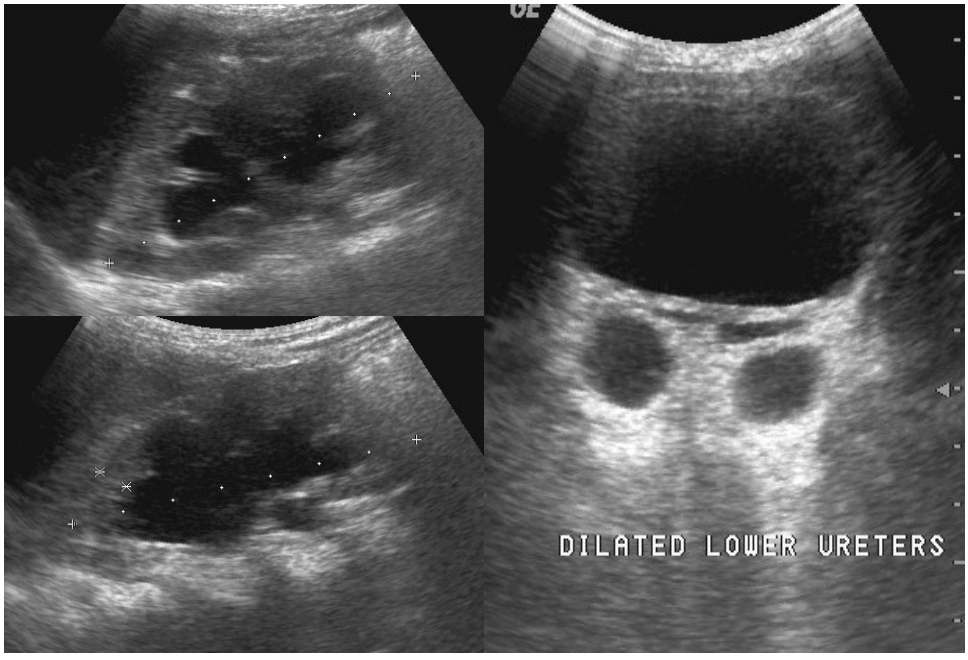
Moderate Hydroureteronephrosis



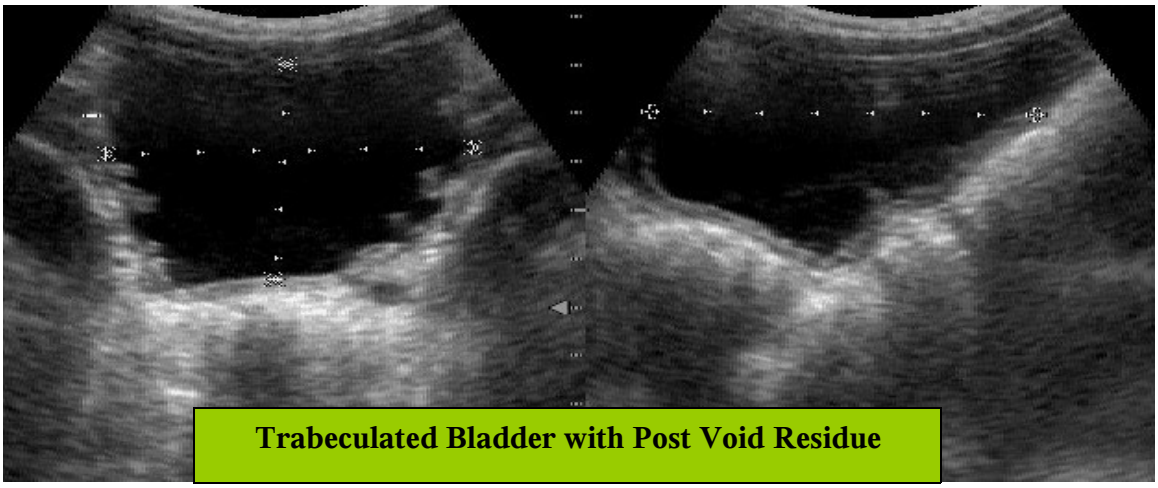
Severe Hydroureteronephrosis



A Child with Non Neurogenic Neurogenic Bladder.

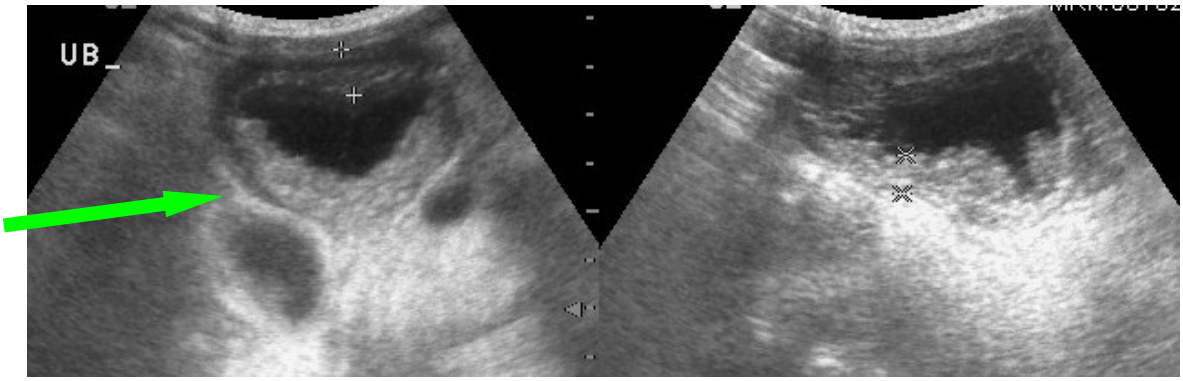


Post void residue was documented sonologically in 8 patients. There was an average residual volume of 59.8ml (range 13-108ml).



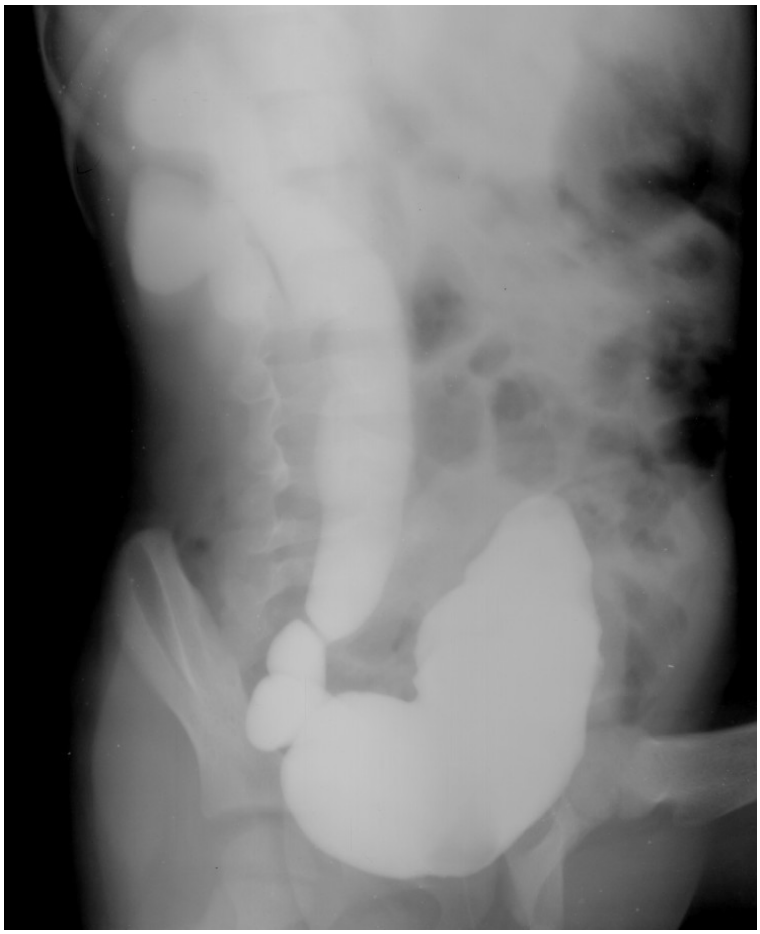
Trabeculated Bladder with Post Void Residue

Bladder Trabeculation was present in all 28 patients. Average wall thickness was 4.85mm (Range 2.9-13mm).



Micturating Cystourethrogram (MCU) [N=28]

MCU showed trabeculation in all 28 patients.9 patients also had elongated bladder outline.



Trabeculated Bladder **(FIR Tree appearance)** with Right Grade V Reflux

56 renal units (in 28 patients) were evaluated for vesicouretric reflux. Reflux was detected in 32 renal units

	Patients	Renal units
Unilateral	N=10	N=10
Bilateral	N=11	N=22

Total	N=21	N=32

SIDE of reflux

Right side	N=18 (13 Gr V, 2 Gr IV, 3 Gr III)
Left side	N=11 (18 Gr V, 3 Gr IV, 2 Gr III, 1 Gr I)

Grades of reflux

Grade I	N=1
Grade III	N=5
Grade IV	N=5
Grade V	N=21
Total	**N=32**

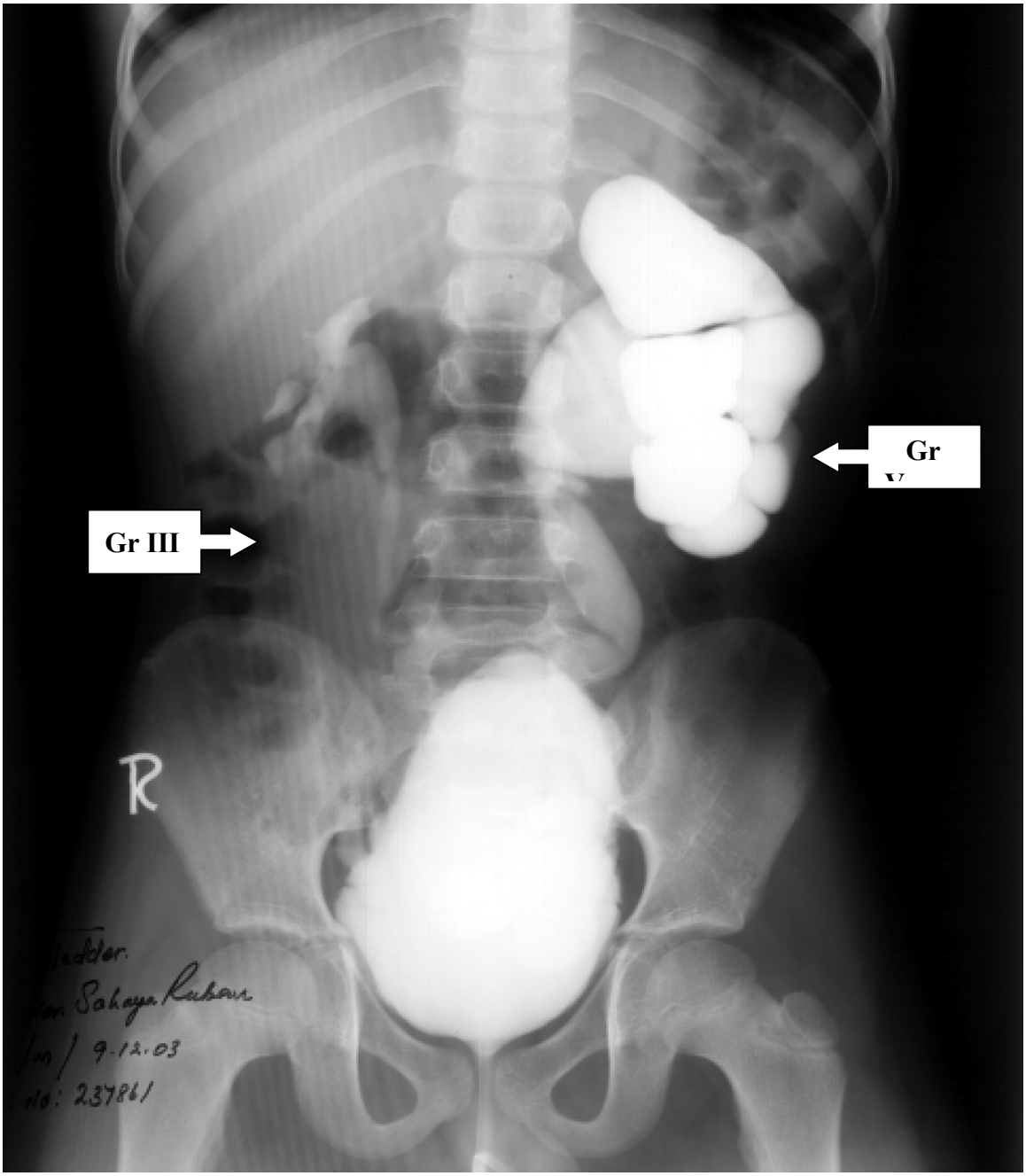
Ultrasound Evaluation of the Contralateral Renal (Non Refluxing) Unit in cases of Unilateral Reflux.

Name	**Contralateral Kidney**
Akash	Mild HUN
Sidharth	Mild HUN
Atul	Mod HUN
Sayani	Normal
Rahul	Severe HUN

Ramya	Mod HUN
Deepak	Normal
Prasad	Severe HUN
Nithya	Severe HUN
Riki	Severe HUN

In the 10 cases with unilateral VUR ,the ultrasound evaluation of the contralateral renal unit revealed HUN in 8 cases(80%). This is an indirect evidence of underlying high pressure bladder which caused VUR on one side along with nonrefluxing dilatation of the other renal unit.

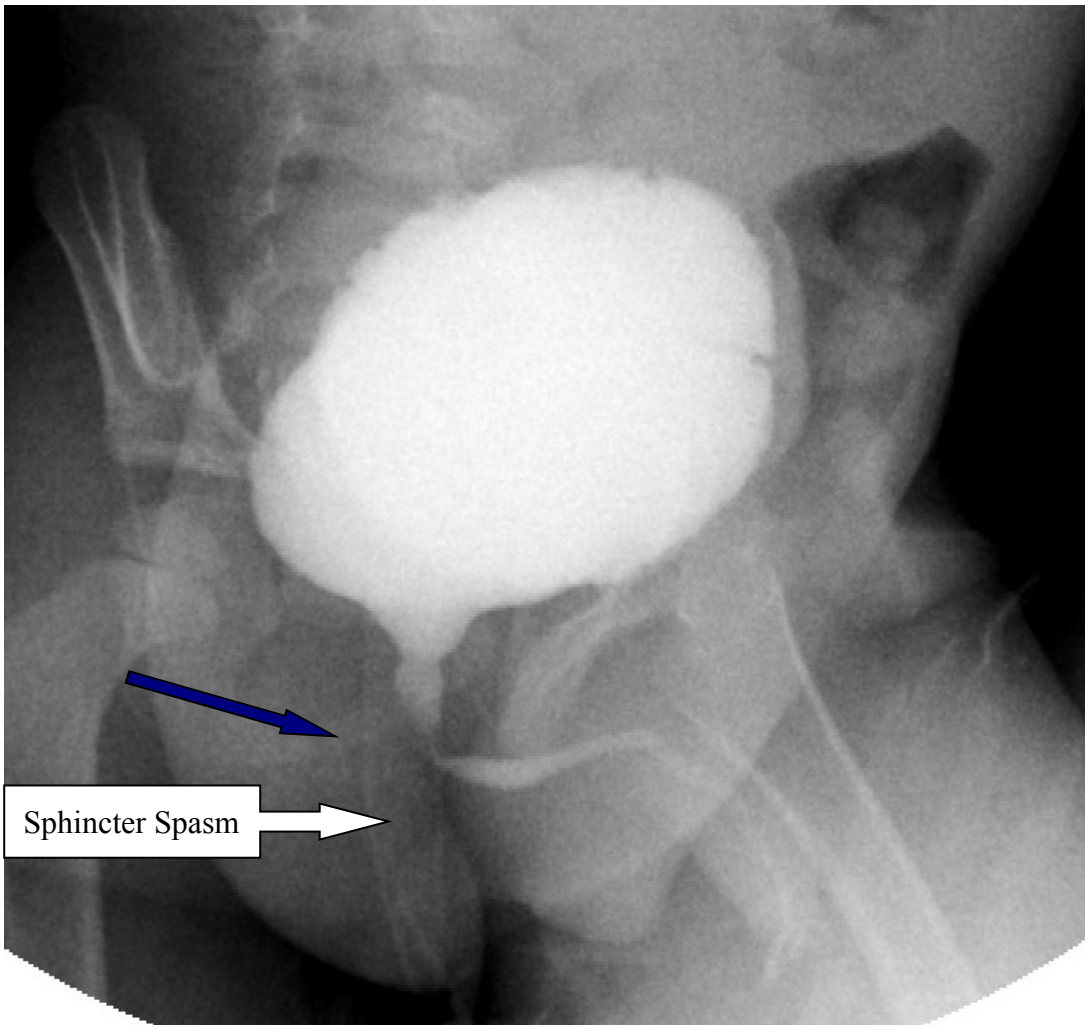
Grade III and V



Bilateral Major Reflux Secondary to Abnormal Bladder

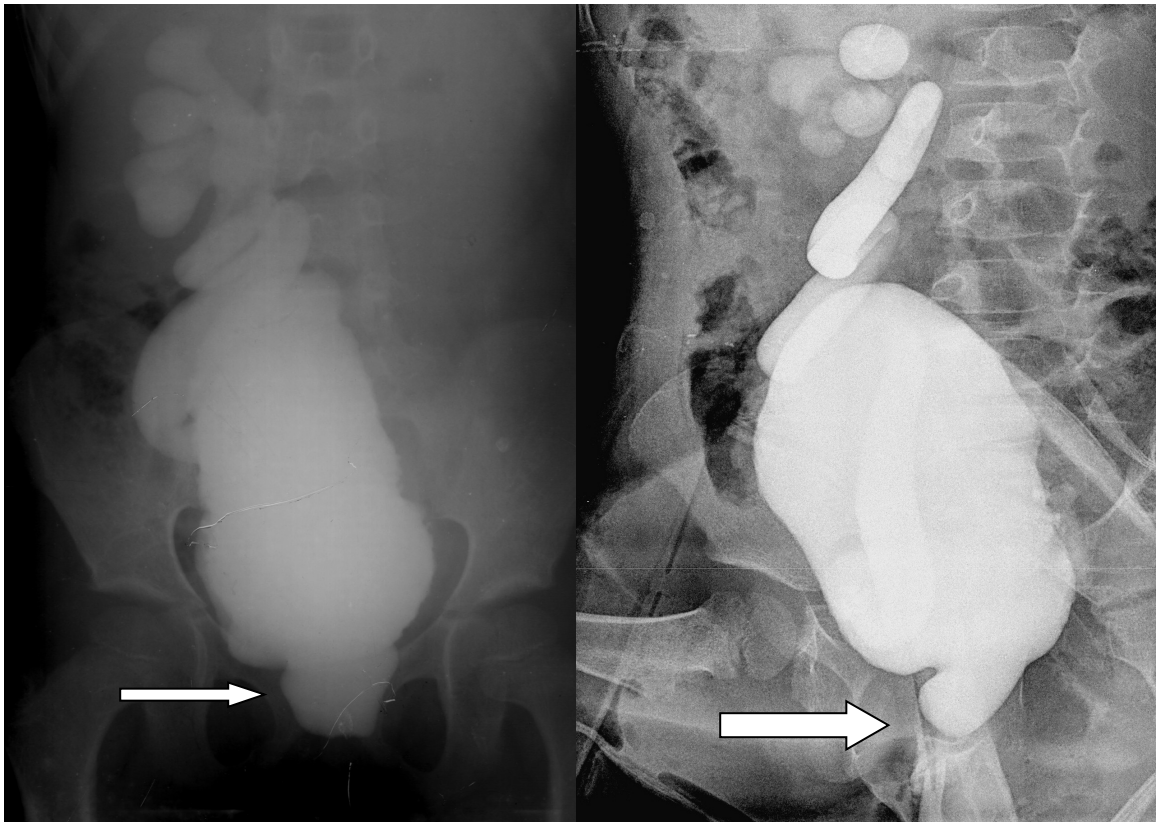
Posterior urethral dilatation in absence in absence of valve is a characteristic finding in patient with detrusor sphincter dyssynergia. This was noted in 13 patients (2 among them girls).

Dilated posterior urethra (Boy)



N= 11

Spinning Top Urethra (Girl)



N=2

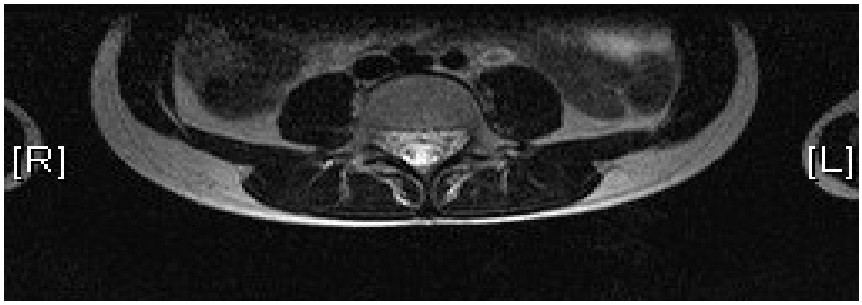
Significant post void residue was noted during MCU in 17 patients.

Spine

Spine was evaluated clinically and with a lumbosacral plain x-ray to document an occult spina bifida. MRI was done selectively in our protocol. Three of our patients who had suspicious cutaneous stigmata of spinal dysraphism underwent MRI. Two had spina bifida occult without

tethered cord, third patient had normal spine.

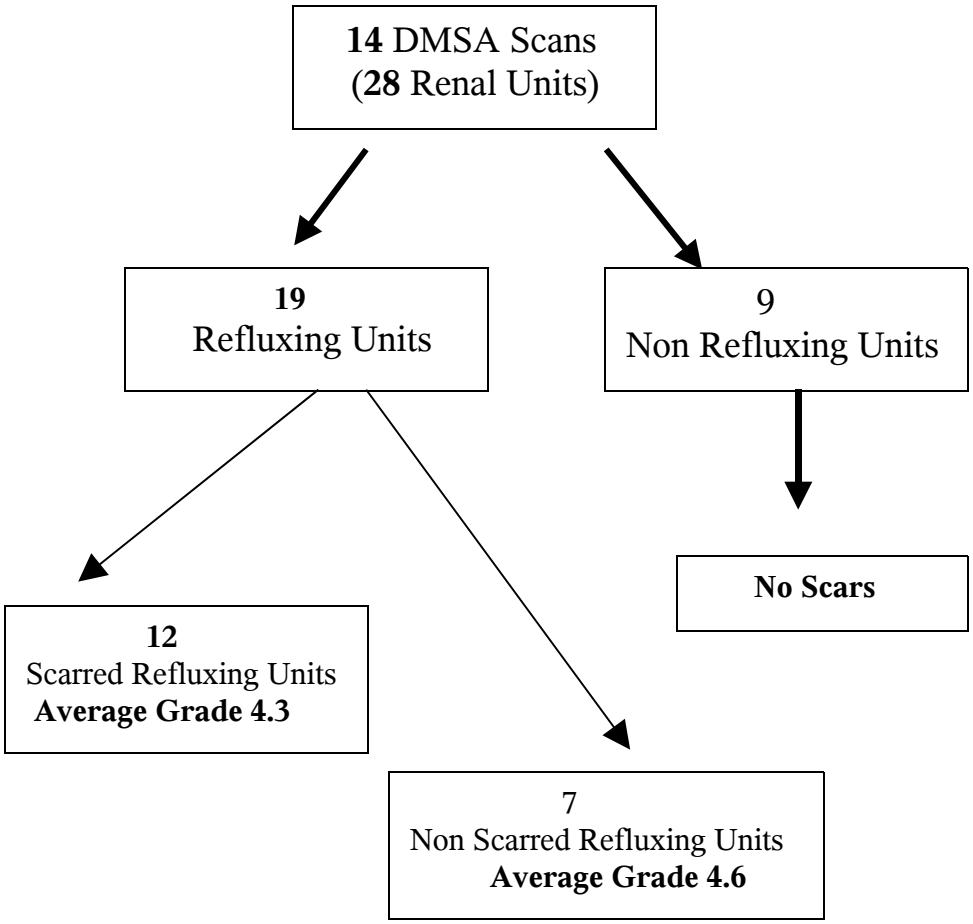
Sacral spina bifida, No tethered cord was seen



Normal Lumbar Spine

Radio nuclear Scan

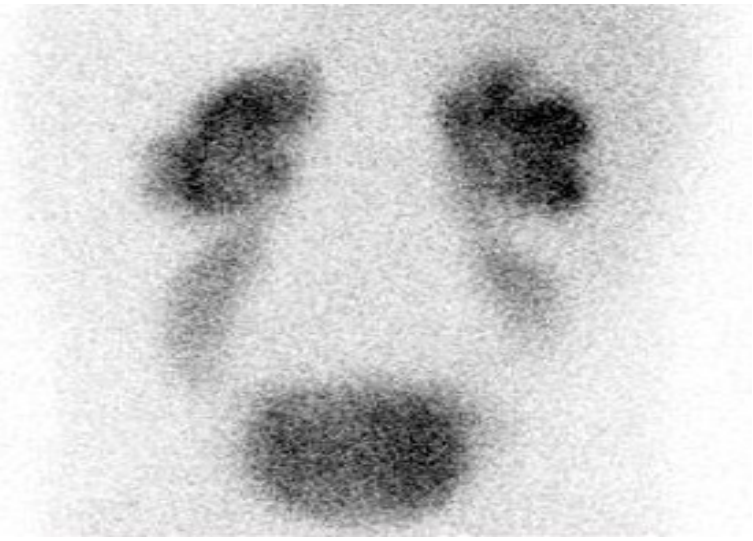
Nuclear renal scan (DMSA) is an important modality of investigation, especially in patients with VUR and history of UTI's. This was done in 14 patients (28 renal units).



Radio nuclear Scan

Small scarred left kidney

Relative function: Left kidney - 21% Right kidney - 79%



Renal cortical scars Right > Left

Urodynamic study

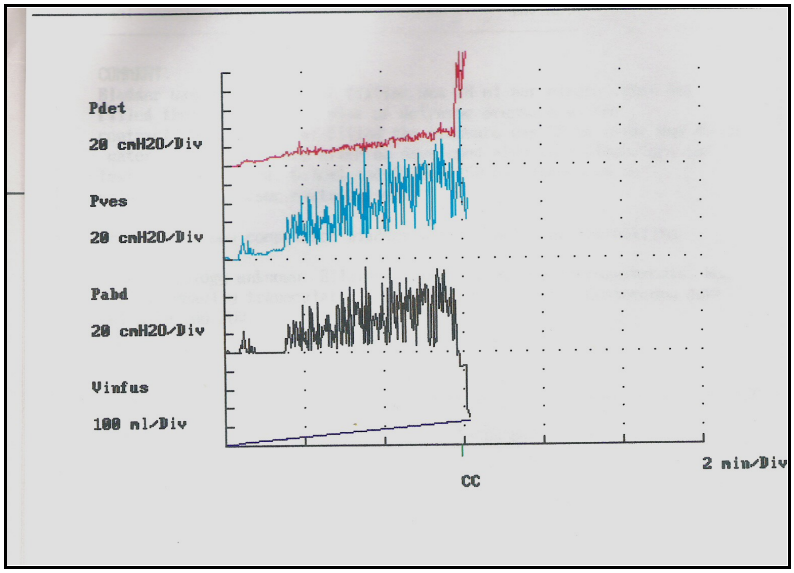
Urodynamic study in patients with lower urinary tract symptoms form an integral part of work up. It influences treatment modality and is an essential tool of

follow-up. 10 patients underwent cystometrogram in our study (as the urodynamic machine was out of order subsequently).

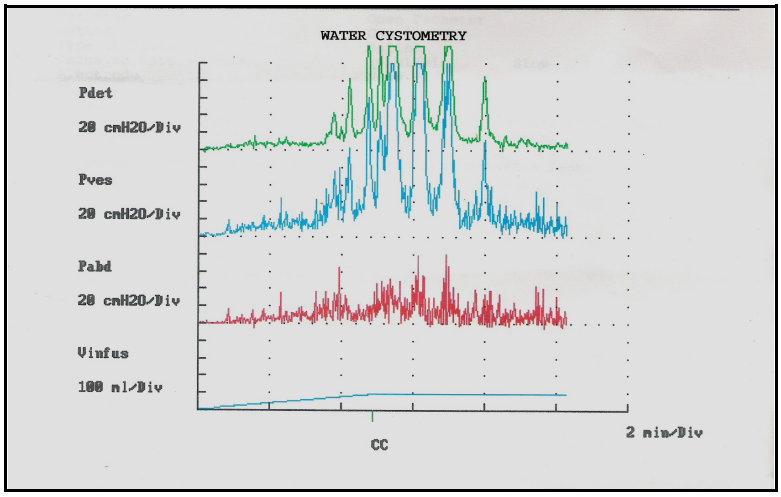
Results of urodynamic study in 10 patients.

Name	**Exp capacity**	**Volume at 20cm H2O(% of exp)**	**Reflux**	**Diagnosis**
Naresh	150ml	136ml (90%)	Nil	Mod compliance, without instability
Riki	180ml	65ml (36%)	Present	High pressure + Det instability
Niranjan	135 ml	70 ml (51%)	Present	Poor compliance, without instability
Sahaya	360 ml	110 ml (30%)	Present	Poor compliance + det instability
Badhon	300 ml	115 ml (36%)	Present	Poor compliance + det instability
Rahul	420ml	420 ml (100%)	Present	Poor compliance + det instability
Ramya	240ml	63 m (26%)	Present	Mod compliance without instability
Saikad	135 ml	100 ml (74%)	Present	Mod compliance without instability
Akash	300 ml	300 ml (100%)	Present	Mod compliance without instability
Keerthana	90ml	35ml (40%)	Present	Poor compliance without instability

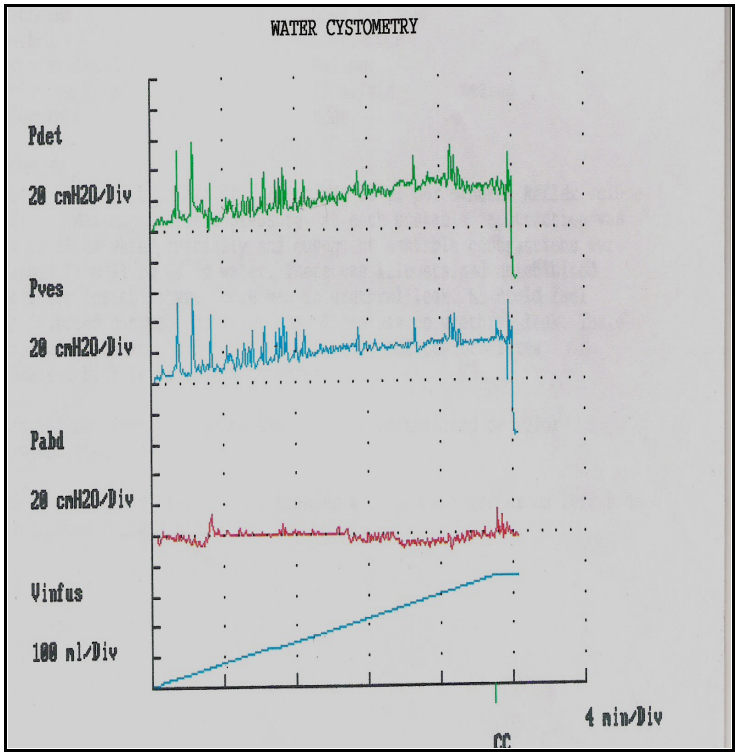
The good compliance patients had major reflux; therefore the “Compliance” is a suspect.



High Pressure Poor Compliance Bladder



Small Capacity Bladder with Detrusor Instability



Poor Compliant Bladder with Detrusor Instability

After laboratory and radiological evaluation child was prepared for surgery. Where ever

possible abnormal parameters were corrected before surgery.

Surgery involved initial cystourethroscopic evaluation followed by definitive procedure.

Cystoscopy (N=26)

Cystoscopy was done using 7.5Fr or 9 Fr Wolff, zero degree rigid scope. None had any evidence of valve or stricture in the posterior urethra. All 26 bladders had varying degree of trabeculation.12 patients had heavily trabeculated bladder, while rest 14 had lesser grade of trabeculation. 52 ureteric orifices were looked for, 28 among them were refluxing.

28 refluxing ureteric orifices- Endoscopic appearance.

Gaping ureteric orifice	N=15
Ureteric orifice not seen	N=6
Normal ureteric orifice	N=7
Total	N=28

<u>Endoscopic appearance of refluxing ureteric orifice.</u>

We have divided the above data into augmented/diverted (advanced bladder pathology) vs non augmented group(less advanced bladder pathology).

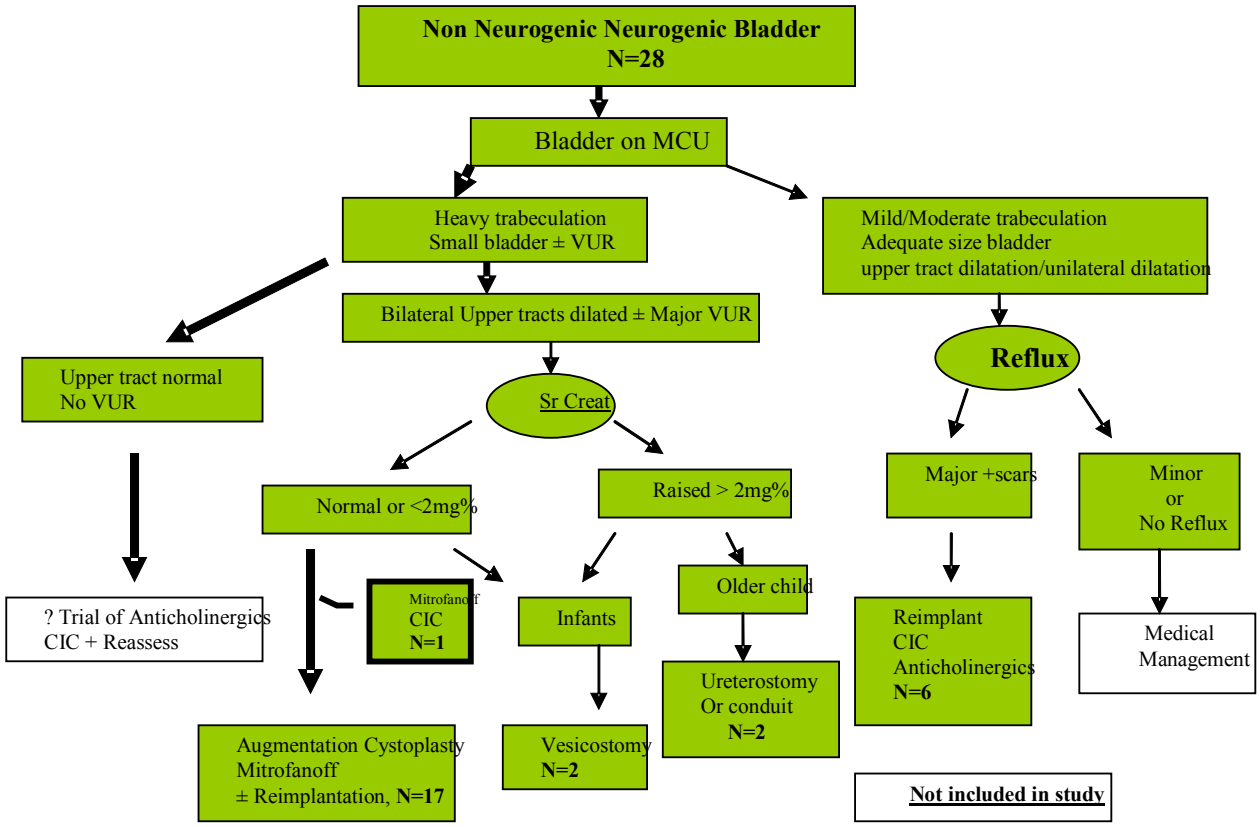
Augmented and Diverted Group (N=18 units)

Gaping ureteric orifice	N=5 (27.7%)
Ureteric orifice not seen	N=6 (33.3%)
Normal ureteric orifice	N=7 (38.9%)

Non Augmented group (N=10)

Gaping ureteric orifice	N=10 (100%)

A “gaping” uretric orifice with VUR was seen in only 27.7% of patients who were augmented/diverted. Thus the VUR was secondary to a high pressure bladder rather than a primary problem at the uretric orifice in many of these units. On the other hand 100% of the refluxing ureter were noted to have a gaping orifice in patients who were not augmented. Thus in many of these there was a problem at the Uretric orifice in addition to a (less advanced) bladder dysfunction when compared to the augmented /diverted group.


Non Neurogenic Neurogenic Bladder
N=28
Bladder on MCU
Heavy trabeculation
Small bladder ± VUR
Mild/Moderate trabeculation
Adequate size bladder
upper tract dilatation/unilateral dilatation
Bilateral Upper tracts dilated ± Major VUR
Upper tract normal
No VUR
Sr Creat
Reflux
Normal or <2mg%
Raised > 2mg%
Major +scars
Minor
or
No Reflux
Mitrofanoff
CIC
N=1
Infants
Older child
? Trial of Anticholinergics
CIC + Reassess
Reimplant
CIC
Anticholinergics
N=6
Medical
Management
Augmentation Cystoplasty
Mitrofanoff
± Reimplantation, N=17
Vesicostomy
N=2
Ureterostomy
Or conduit
N=2
Not included in study

Definitive Treatment (Surgical procedure)

Definitive surgical procedure was guided by degree of hydronephrosis, presence of reflux and renal function.

Treatment algorithm was created based on the above factors.

Procedure are classified into 4 broad categories

1) Reimplantation ± continent catheterisable channel. (N=6)

   Without Augmentation
2) Continent catheterisable channel (Mitrofanoff) alone. (N=1)
3) Augmentation +Mitrofanoff ± antireflux procedure.(N= 17)
4) Diversions (temporary/permanent) (N=4).

Details of definitive procedure are as follows.

a) Reimplantation ± Mitrofanoff without Augmentation

N= 6

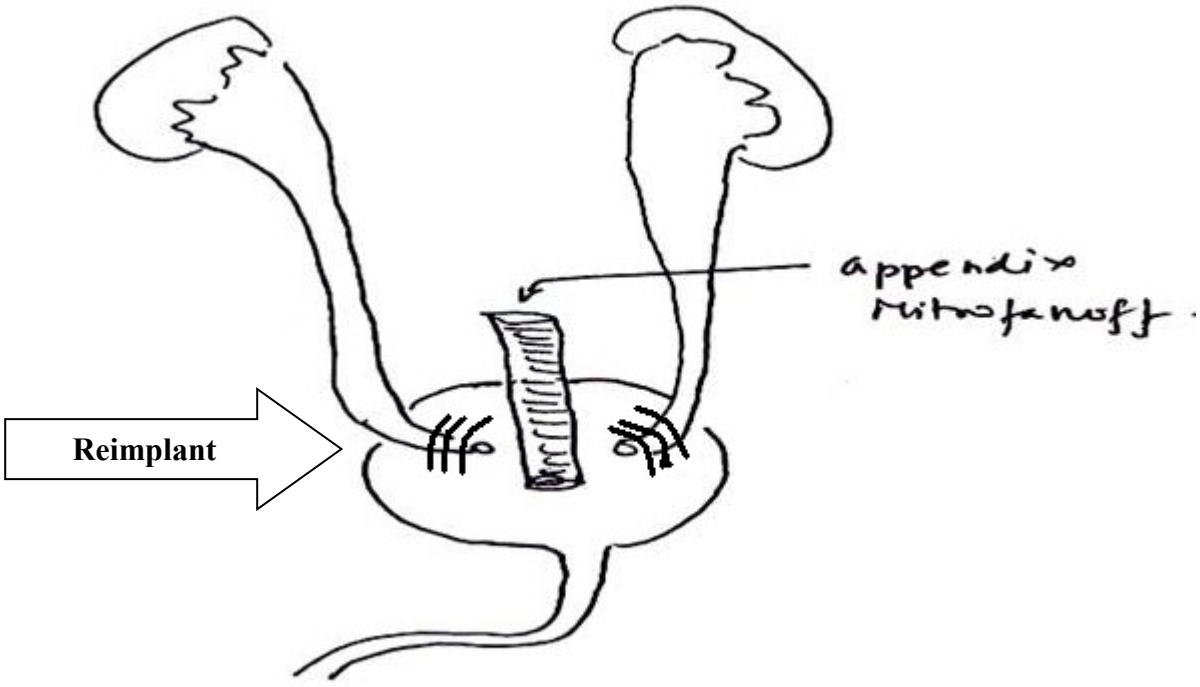
Major reflux secondary to dysfunctional voiding does not resolve spontaneously and causes increased scarring. Reimplantation alone is inadequate and will result in deterioration of renal function. These bladders which are primarily at fault require drugs (Anticholinergics) as well as intermittent catheterization to prevent over activity.

Adding a catheterisable channel for the purpose of CIC is an useful adjunct in these subset

of patients. Although CIC can be done per urethra, mitrofanoff procedure provides a painless route of CIC.

Reimplantation alone+ Urethral CIC	N=1
Reimplantation +Mitrofanoff	N=5
Total	N=6

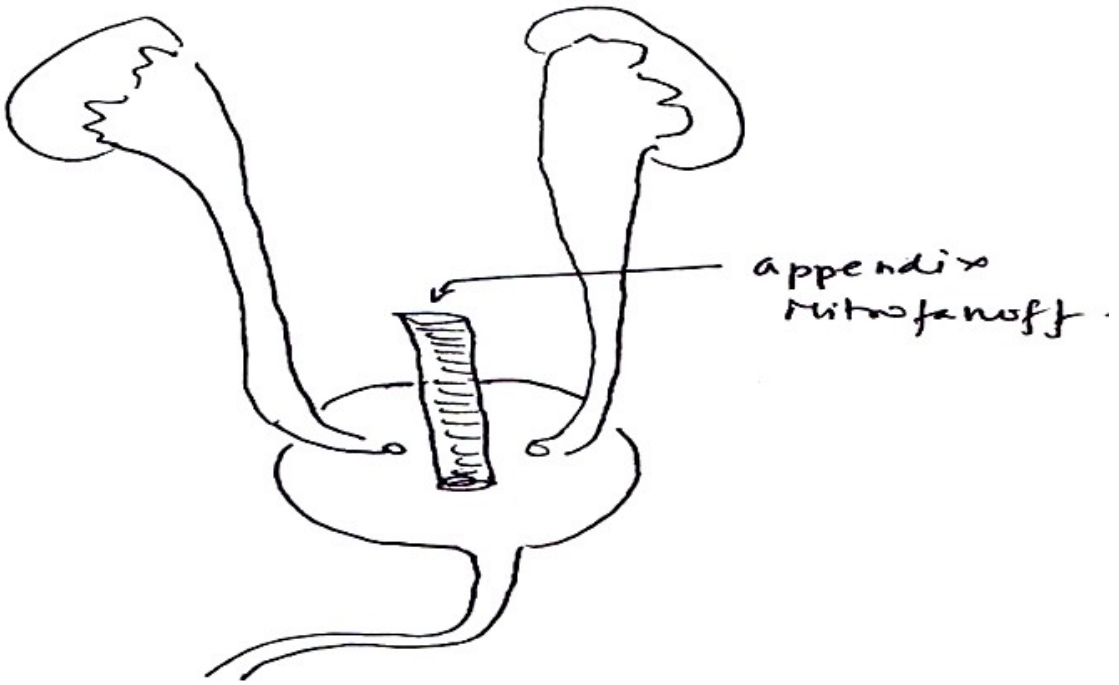
Reimplantation with Appendicular Mitrofanoff.



b) Continent Catheterisable Channel Alone (N=1).

Patient presenting with minor degree of trabeculation, significant post void residue in absence of reflux requires Anticholinergics and effective bladder drainage. A

3 years old boy presented with history of dribbling, recurrent UTI and urinary retention. Radiological investigation revealed bladder trabeculation and moderate bilateral Hydroureteronephrosis in the absence of reflux with significant PVR. MCU and Cystoscopy ruled out posterior urethral valve. He underwent a CMG which showed a safe bladder capacity of 136 ml (90% calculated capacity) at 20 cm H2O. Clean intermittent catheterization is the treatment of choice. Hence an appendicular mitrofanoff was created for painless CIC.



c) Augmentation +Mitrofanoff ± antireflux procedure

N=17.

Justification of the procedure

Children with major upper tract dilatation with or without VUR and in the presence of poor compliant bladder are managed with Augmentation Cystoplasty and clean intermittent catheterization. CIC alone is not sufficient in presence of small capacity, high pressure bladder with severe upper tract dilatation.

Guiding principle in the management of reflux during Augmentation

Management of a refluxing ureter during augmentation is determined by factors like nature of uretric orifices, bladder trabeculation and grade of reflux. Although an augmentation alone is sufficient for reflux resolution in a high pressure system, a dilated uretric orifice in a non compliant bladder may not always resolve with augmentation alone. Reimplantation into the native bladder is the first choice, if this can be safely done (these severely trabeculated bladder may be a limiting factor). In case of an unilateral reflux where the contralateral ureter is dilated, a Transuretero-ureterostomy (TUU) is an acceptable technique of reflux management. Reimplantation into the bowel, in the form of a nipple can be undertaken when above mentioned options are not available. A severely dilated, tortuous ureter can be used for augmentation either with a

TUU in case of a functioning kidney or with a nephrectomy if the kidney is nonfunctioning.
16 refluxing units were managed in the augmented patients of which all except 1 were high grade reflux.

Anti reflux technique in Augmented patients (16 renal units with VUR).

Reimplantation into bladder	N=7
Transureteroureterostomy to contralateral dilated but nonrefluxing ureter	N=6
Reimplantation into the bowel portion of augment	N=1
Augmentation alone	N=2

An augmented bladder cannot empty effectively. Clean intermittent catheterization is required to drain the urine at routine interval. This can be performed per urethra, via a catheterisable stoma created from an implanted appendix or lower end of a refluxing ureter (where TUU has been done). This stoma is also required for continuous night drainage and daily bladder wash.

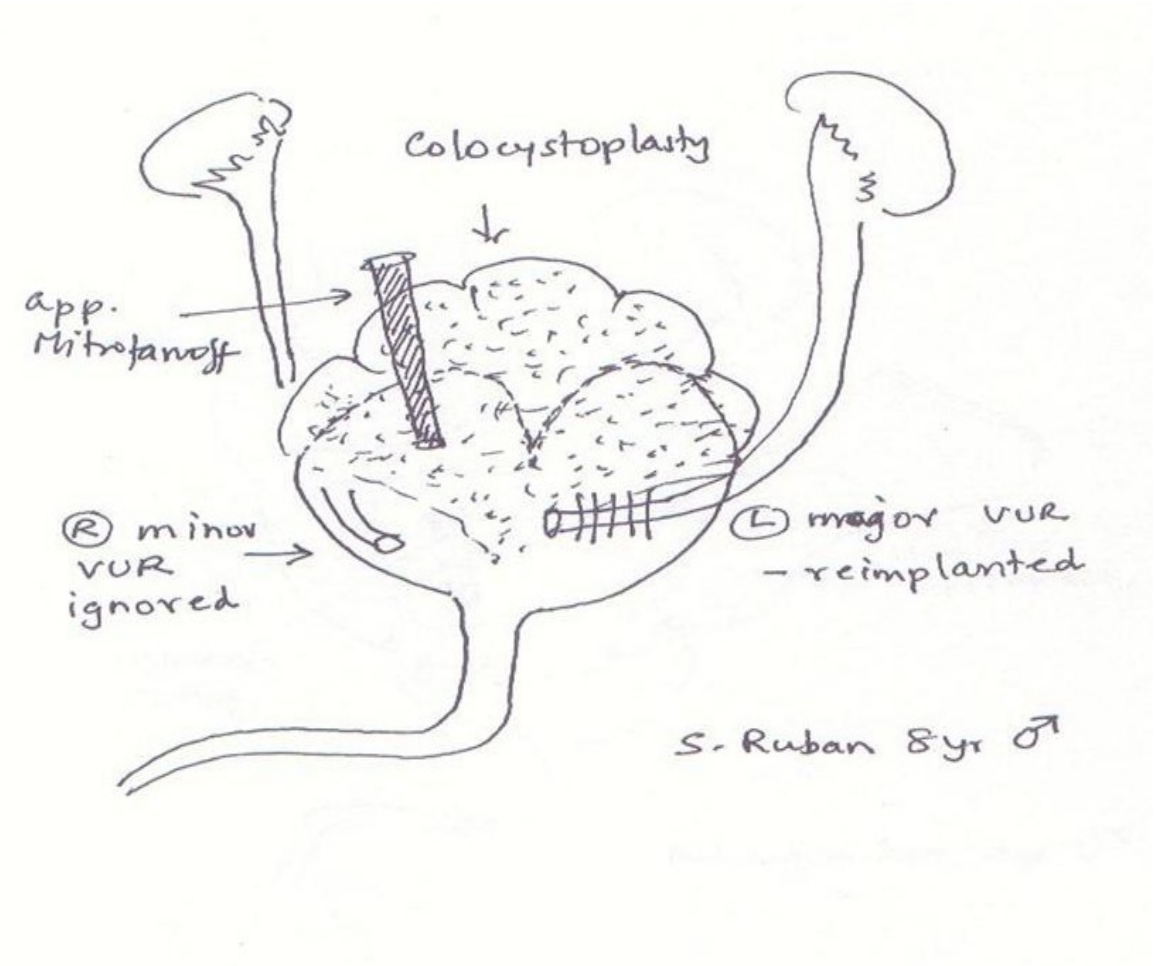
Catheterisable channel in 17 Augmented patients.

Appendix	N=12
Uretric	N=4
Dual	N=1

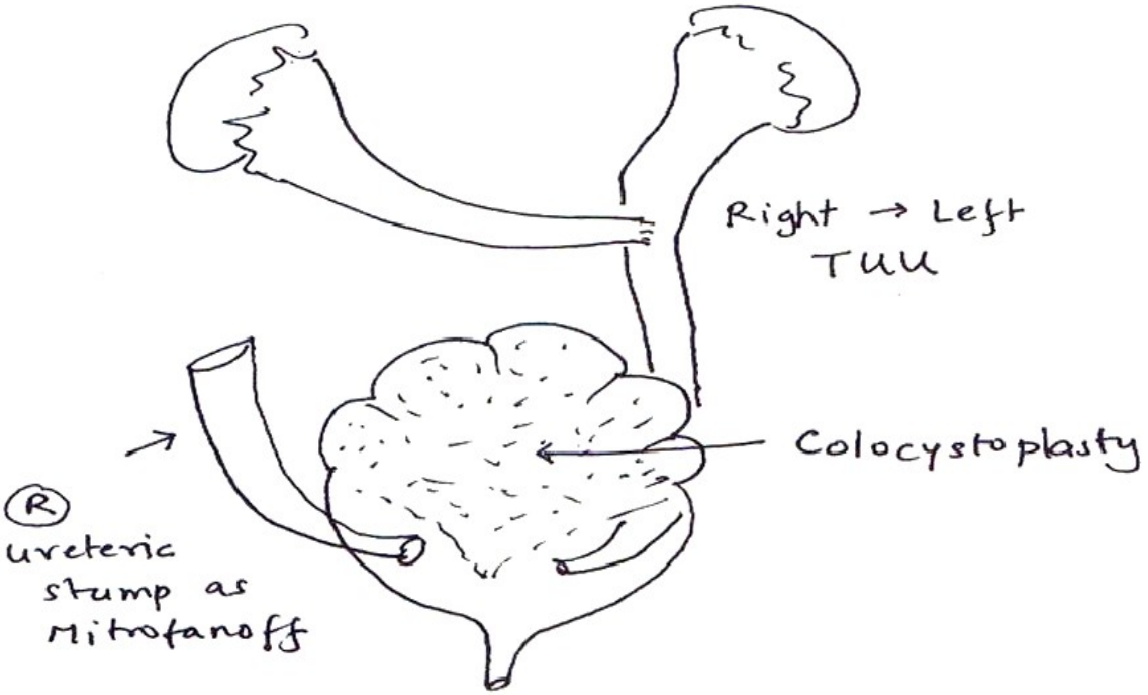
Augmentation Techniques.

Regular intraabdominal sigmoid colocystoplasty	N=6
Extraperitoneal sigmoid colocystoplasty	N=7
Ileocystoplasty	N=1
Ureterocystoplasty	N=2
Auto augmentation	N=1
Total	N=17

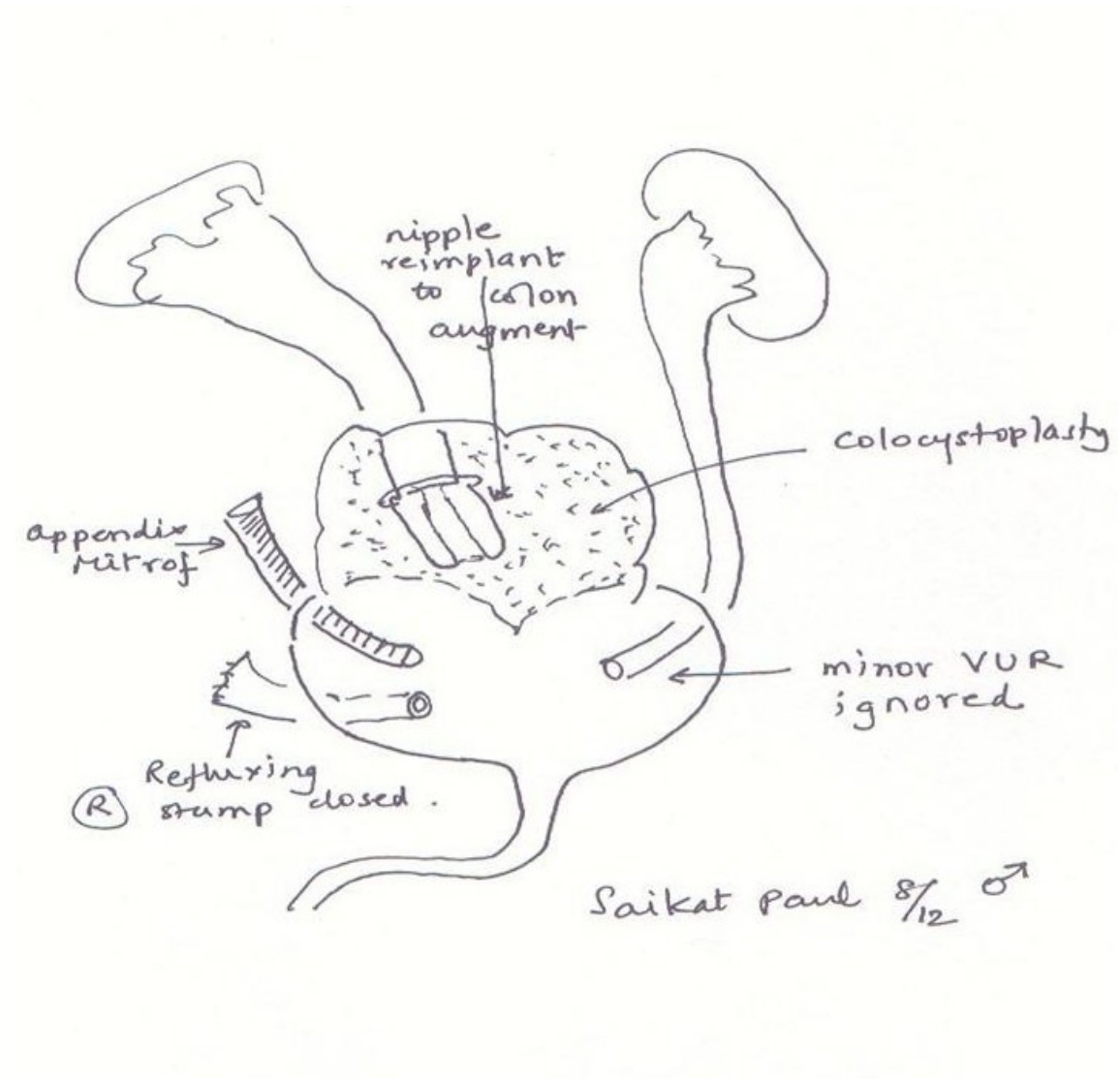
Classical Sigmoid Colocystoplasty with antireflux procedure and appendicular mitrofanoff



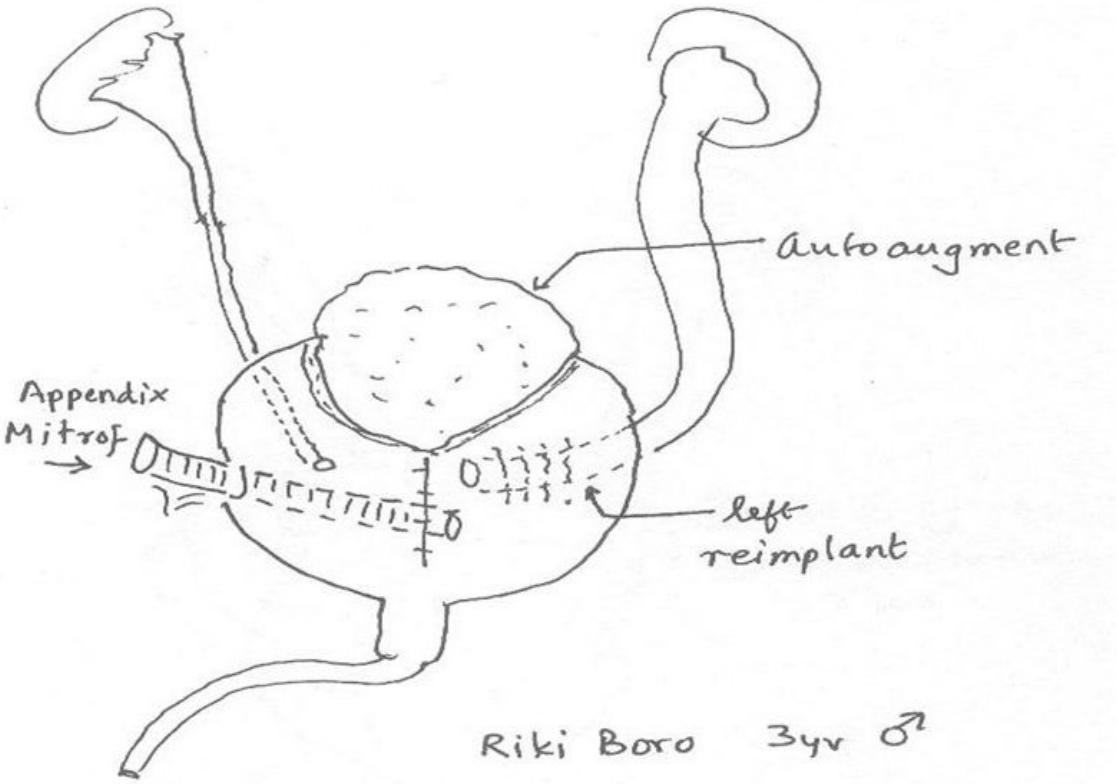
Colocystoplasty with TUU and Ureteric Mitrofanoff.



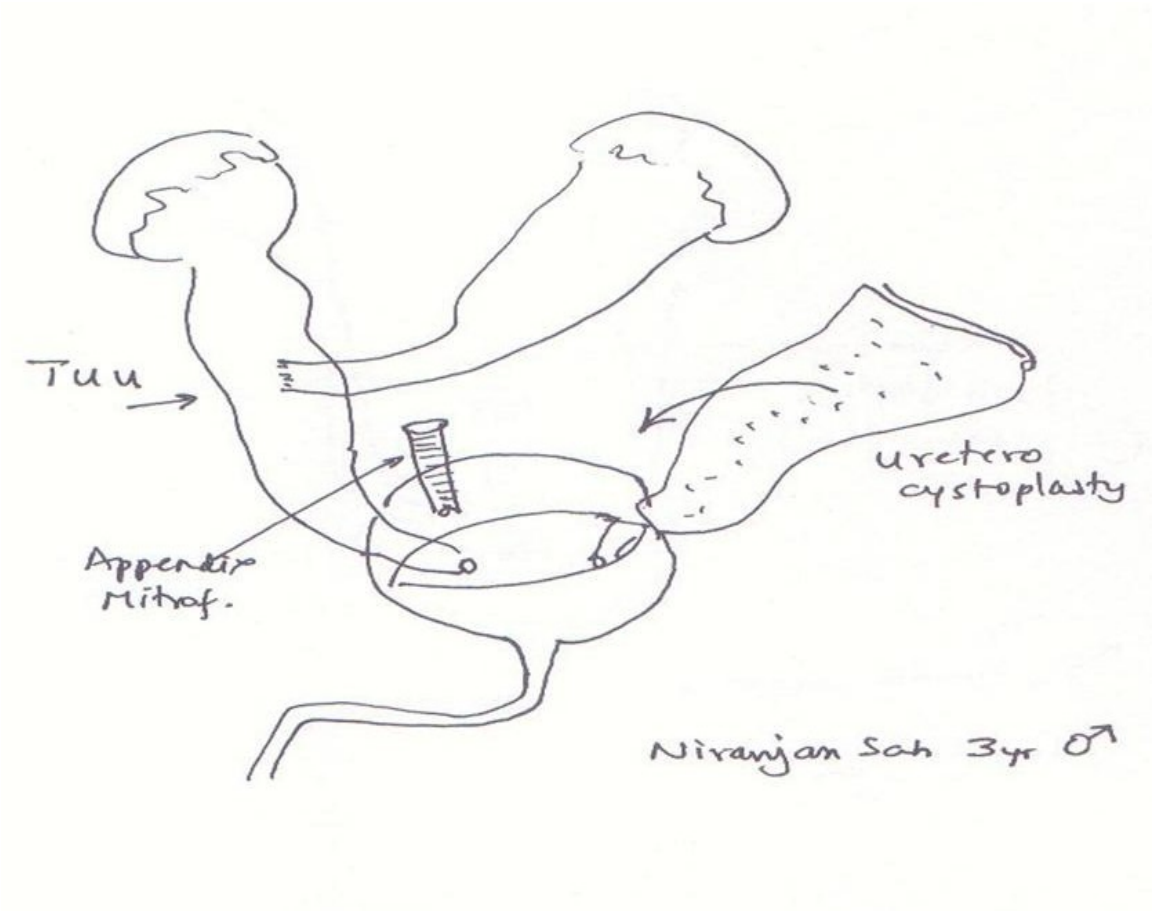
Augmentation + Antireflux procedure + Mitrofanoff.



Autoaugmentation + antireflux procedure + Mitrofanoff



Ureterocystoplasty + TUU + Appendicular Mitrofanoff



d) Diversion

↓

n= 4

Diversion is indicated in presence of urosepsis and chronic renal failure.

In an acute event like urosepsis an emergency temporary diversion like a vesicostomy or ureterostomy can be lifesaving. In contrast a chronic renal failure requires a permanent resistance free diversion till a renal replacement is ready.

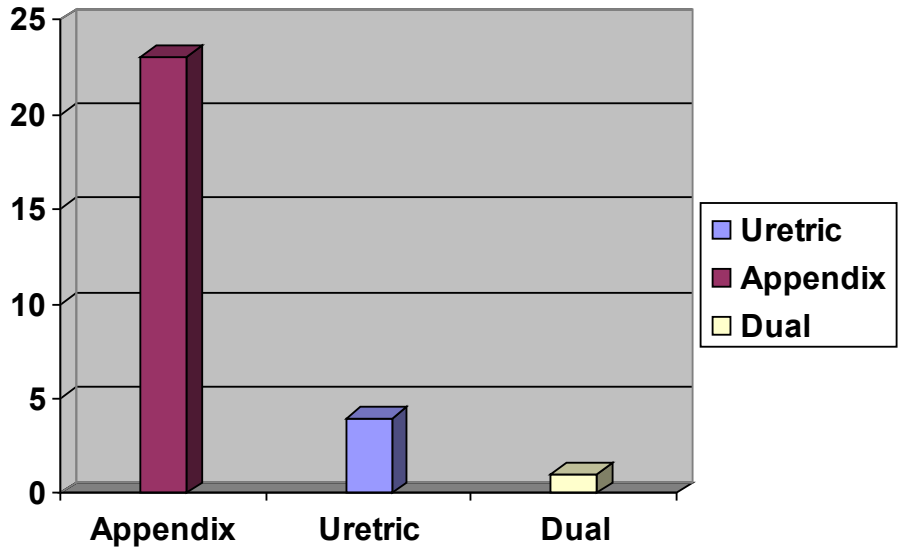
We had 4 cases that required diversion.

Temporary Diversion	
Ureterostomy, age : 5 year old	N=1, urosepsis, S.Creat : 1.9 mg%
Vesicostomy, age : 1 Year & 8 months	N=2,urosepsis, Avg Creat 1.45 mg%
Permanent Diversion	
Ileal conduit , 11 year old	N=1,Chronic renal failure (4.5 mg%)

Catheterisable Channel: An overall assessment.

Catheterisable channel (Mitrofanoff) to evacuate residual urine is an important component of complex urological reconstruction. 23 of our patients had a mitrofanoff channel.18 of them were constructed using appendix. While 4 were the distal ureter of a TUU procedure, one

patient had both appendicular and uretric mitrofanoff. All 17 augmented patients had a mitrofanoff channel, while in the reimplantation group 5 patients had this procedure.



Average duration of follow-up (n=25) in this study was 2.45 years (0.5-9 years).

Results

Dysfunctional voiding is a commonly treated condition in this institute. While majority are treated non operatively, 28 patients were identified who required surgical intervention. Patients were categorized depending on the surgical treatment into 4 broad groups

1) Reimplantation ± Mitrofanoff without augmentation.
2) Continent catheterisable Channel alone (Mitrofanoff).
3) Augmentation + Mitrofanoff ± Antireflux procedure.

4) Diversion.

Results of surgery in each group were analysed in terms of resolution of symptoms, Hydroureteronephrosis, reflux and stabilization of renal function.

1) Reimplantation without Augmentation (but with CIC ± Anticholinergics)

6 patients presented with predominantly major reflux secondary to disturbed bladder dynamics.

Symptoms

Two patients had recurrent episodes of UTIs requiring intravenous antibiotics.

Reflux resolution

There were 10 refluxing units for antireflux procedure .Follow-up MCU was available in 7 renal units (5 Patients) for an average duration of 10.5 months (5mths-21mths).

There was complete reflux resolution in 5 units (71%). 1 non dilated refluxing uretric orifice (managed conservatively) continued to reflux. One refluxing unit had a failed reimplant.

Hydroureteronephrosis

Ultrasonographic evaluation of 10 renal units in this group at follow-up showed decreased Hydroureteronephrosis in 7 units, whereas 3 renal units were stable.

Creatinine

None of the 6 patients had raised preoperative serum Creatinine.

Average preoperative serum Creatinine was 0.76mg% in this category, while post operative Creatinine was 0.71mg%.

Post operative complication

Transient leak at supra pubic cystostomy site was found in a patient who did not undergo a mitrofanoff procedure. This was managed with anti-cholinergic and urethral catheterization

CIC

All the patients are compliant with intermittent catheterization. 1 patient is doing urethral CIC while rest using their mitrofanoff port for intermittent catheterization
and night drainage.

2) Continent Catheterisable Channel

1 patient presented with trabeculated bladder, dilated upper tracts (No VUR) and significant residual urine. He underwent mitrofanoff procedure for CIC. At follow up after 6.5 years, he showed remarkable resolution of Hydroureteronephrosis as well as bladder trabeculation. He had an episode of cystitis which required intravenous antibiotics.

3) Augmentation + Mitrofanoff ± Antireflux procedure

17 patients underwent Augmentation Cystoplasty.

a) Symptoms

16 out of 17 patients had a follow up of average 2.8 years (range 6 mths-9yrs).

All are free of their preoperative presenting symptoms i.e. dribbling, retention.

All patients are regularly doing clean intermittent catheterization. 1 patient has occasional pain radiating to penis while catheterizing the mitrofanoff. 1 chilld is lost to followup. She had a high Creatinine and is probably expired.

b) Infection

3 patients have history of recurrent urinary tract infection requiring admission and intravenous antibiotics. This is probably related to irregular emptying of neobladder. 1 patient with a colonized bladder has been treated with antibiotics and bladder drainage.

c) Serum Creatinine

Pre-operative serum Creatinine in this group ranged from 0.5 to 3.1 mg% overall an average of 0.95 mg%.

Post operative serum Creatinine showed a drop to an average of 0.8mg % (Range 0.5-1.3mg %).

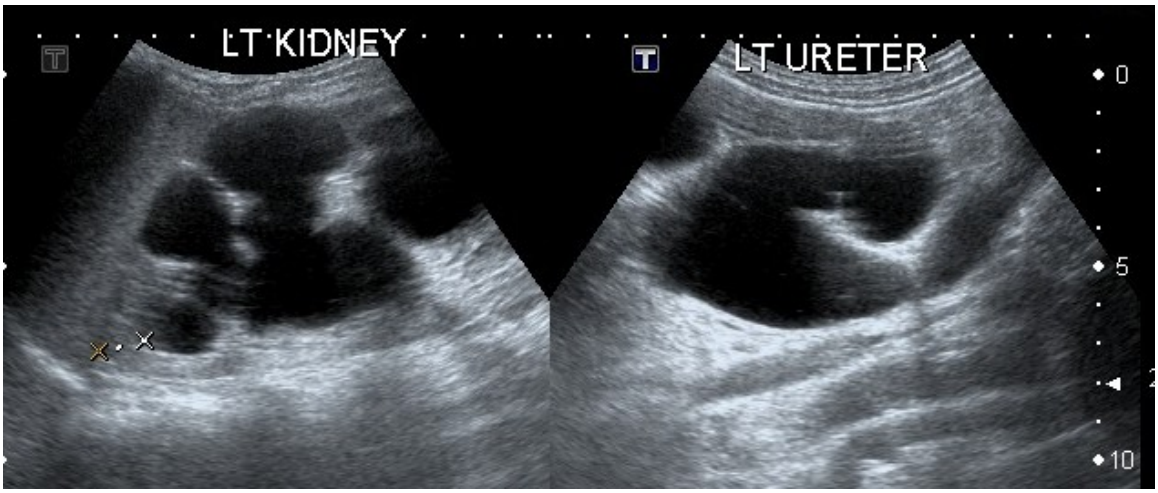
5 Patients with raised pre operative serum Creatinine (Average 1.6 mg %). At follow up they had an average value of 0.96 mg%.

d) Hydroureteronephrosis

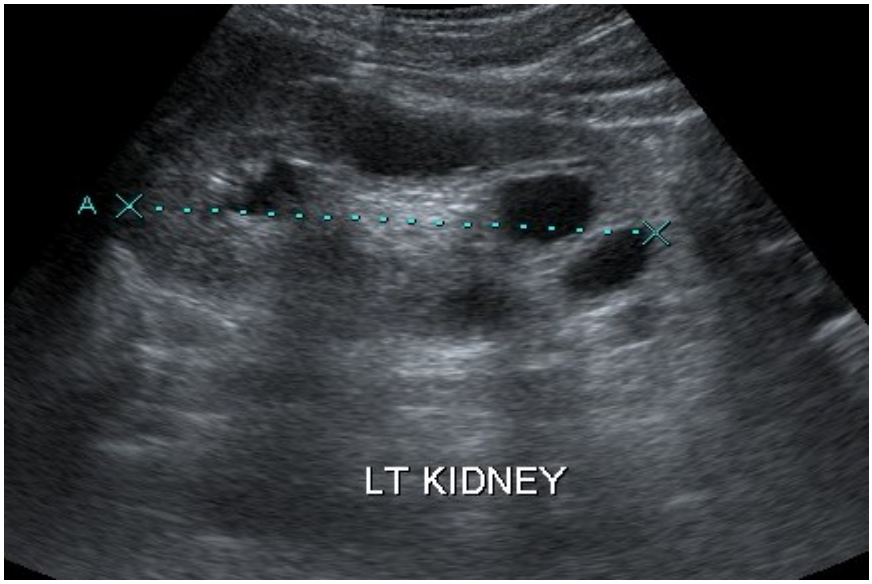
Preoperative severity of Hydroureteronephrosis of each renal unit was compared with the post op image.

30 renal units were dilated preoperatively. At follow up 22 renal units showed significant decrease while 6 had stable Hydroureteronephrosis. 1 patient with serum Creatinine of 3 at discharge is yet to follow up, she is probably no more and has been excluded in the analysis.

Hydroureteronephrosis



Pre Augmentation Cystoplasty



Post Augmentation Resolution of Hydroureteronephrosis

e) Result of Reflux management in Augmented patients.

Major reflux is an important indication of surgery in this group of patients.

We had 16 refluxing units to treat in this modality.

13 preoperative refluxing units in this category were reviewed with post op MCU.

N=5	Reimplantation into bladder	100% resolution
N=5	TUU	100% Resolution
N=1	Reimplantation into Bowel(NIPPLE)	Reflux resolved
N= 2	Augmentation alone	Reflux resolved

Techniques of Reflux management during Augmentation Cystoplasty

Small Capacity Bladder
with Right Grade V Reflux
and Creatinine of 1.5 mg%

Ureterocystoplasty + TUU

Post **Ureterocystoplasty** and TUU
Improved bladder capacity and reflux resolution. Creatinine 1.2 mg%

Techniques of Reflux management during Augmentation Cystoplasty

12 year old boy with LUTS and Right major VUR

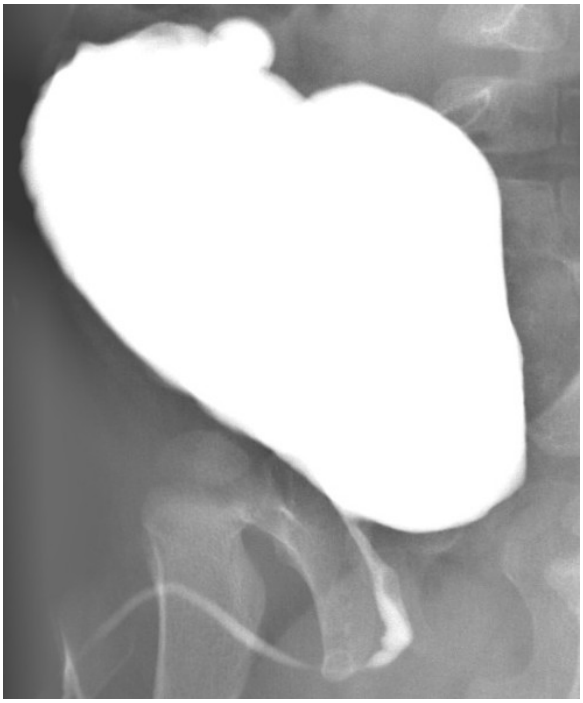
Augmentation Alone.

Resolution of major VUR with Augmentation alone

Techniques of Reflux management during Augmentation Cystoplasty

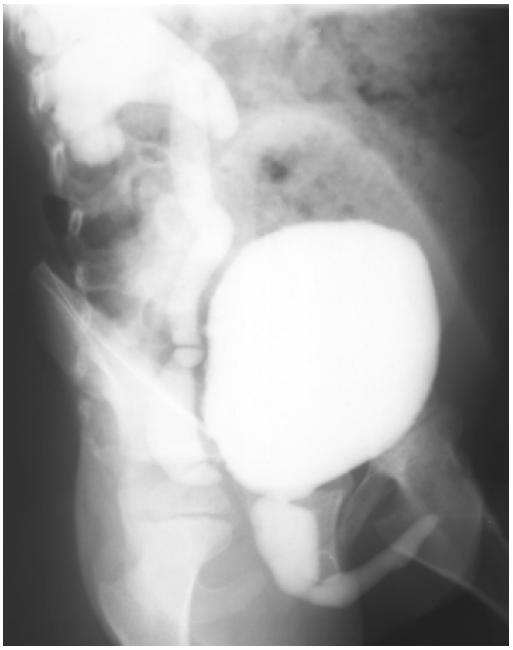
Bilateral VUR

Right Nipple Reimplantation into Bowel portion of Augment & Left VUR left alone



No VUR

Techniques of Reflux management during Augmentation Cystoplasty



Right VUR with retention

Reimplantation into Bladder with Autoaugmentation + Mitrofanoff

No VUR

f) Complications

Early

Adhesive intestinal obstruction requiring laparotomy	N=1
Bleeding	N=1
Burst abdomen	N=1
Mitrofanoff stoma dehiscence	N=1
Neocystocutaneous fistula	N=1

Late

Neobladder Spontaneous Perforation	N=1
Adhesive obstruction	N=1
Calculi	N=1
Mitrofanoff stoma stricturing	N=1

4) Diversion

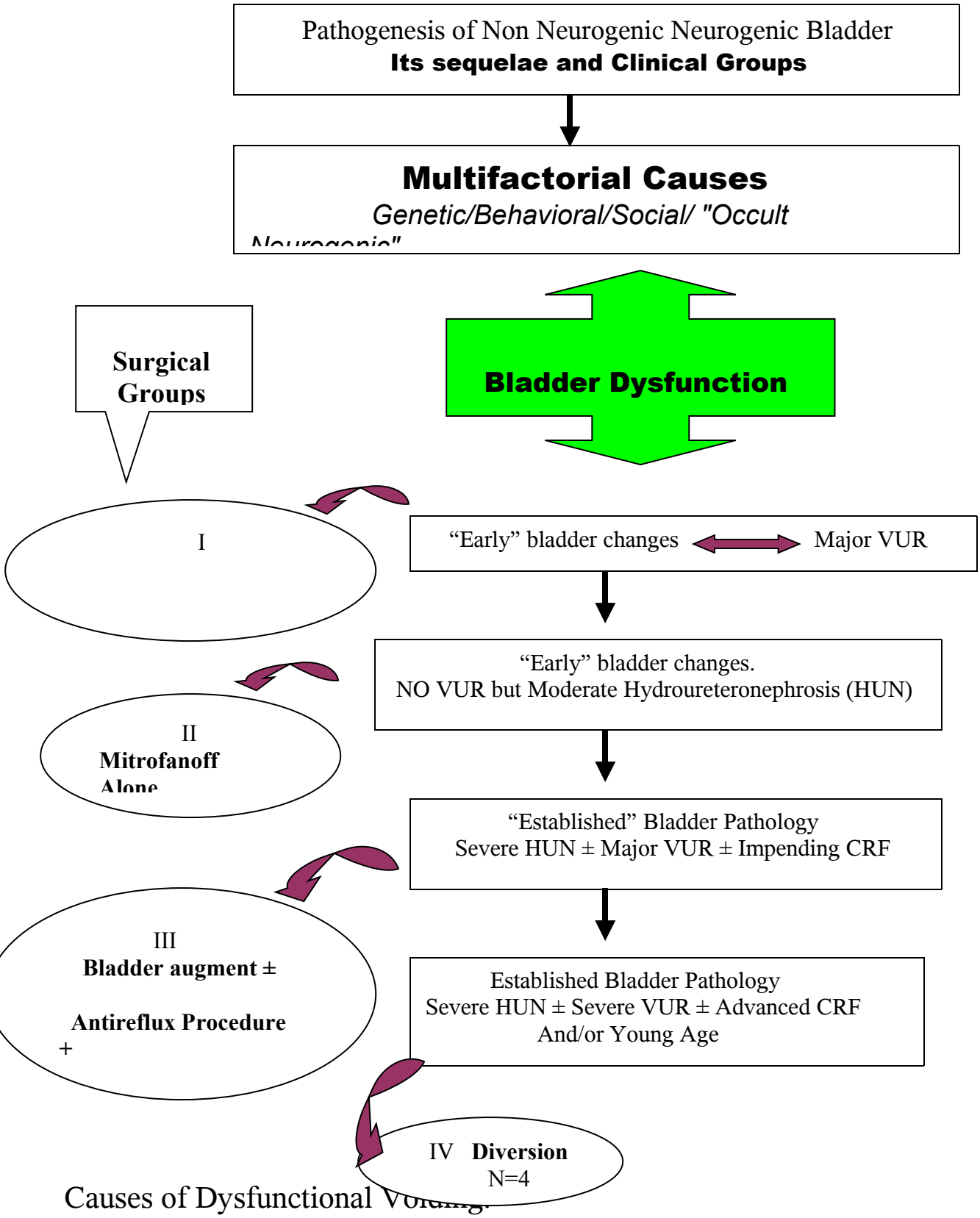
In the Vesicostomy group average Creatinine dropped from 1.45mg% to 0.5mg%

The child who underwent ileal conduit too showed significant recovery, his Creatinine decreased from 4.5 mg% to 1.7mg%.

At follow-up Hydroureteronephrosis was found to be stable in 3 renal units while it showed a reduction in 3 unit.

One patient is awaiting follow-up.

Discussion



Causes of Dysfunctional Voiding:

Dysfunctional voiding in neurologically and anatomically normal children is defined as inappropriate functional contraction of pelvic floor and external sphincter muscle during voiding leading to bladder outlet obstruction. It causes incontinence, urinary tract infection, difficult urination, residual urine and upper tract deterioration.

Dysfunctional voiding syndrome is a heterogeneous entity. There is a wide spectrum of its clinical and radiological manifestation. At the milder end are patients who have lower urinary tract symptoms with minimal bladder and upper tract changes. While at the severe end, detrusor sphincter dyssynergia results in gross upper tract dilatation and renal damage. Only these patients qualify as having **Non Neurogenic Neurogenic Bladder**.

Non Neurogenic Neurogenic Bladder was first described in 1915 by Beer, who stated that “the condition is frequently one of disharmony between the detrusor and sphincter muscle or relative hypertonicity of the sphincter.

Hinman, 1973 whose name is synonymous with this condition was first to emphasize the importance of psychological factors in this condition. He said, “It is useful clinically to think of it as a bad habit that develops in children of certain personality types in an unfavorable family setting”. Others believe it is learning disorder during school age. Infants with features of Non Neurogenic Neurogenic Bladder has been reported in the literature. Given the young age of the patients it is unlikely that social factors are involved, thus bladder dysfunction must be the

primary problem. Controversies still exist as to whether a very subtle or occult spinal pathologic process can occur to account for an isolated bladder neuropathy in a child who does not exhibit other somatic neurologic deficits and has normal magnetic resonance

imaging of the spinal cord

An indirect evidence that a very subtle or occult neurologic lesion may account for some cases of “non-neurogenic neurogenic” bladder-sphincteric dysfunction is the Ochoa (urofacial) syndrome. Children with this syndrome exhibit all the classic features of dysfunctional voiding, including urinary incontinence, recurrent UTIs, constipation, reflux, and upper tract damage, but they also have a peculiar painful or apparently crying facial expression during smiling (Ochoa and Gorlin, 1987 ; Ochoa, 1992). The condition has an autosomal recessive inheritance, and the gene has been located on chromosome 10 (19). Because the neural ganglia controlling the facial muscles are situated very close to the pontine micturition center, it is tempting to speculate that a small genetically predetermined, congenital neurologic lesion in this area may be responsible for both the peculiar facial expression and the bladder dysfunction. Further studies in this direction may help to resolve some of the continuing dilemma

Diagnosis of Non Neurogenic Neurogenic bladder in our cases.

Diagnosis of a Non Neurogenic Neurogenic bladder depends on demonstration of bladder trabeculation and its sequelae (upper tract dilatation) in neurologically and anatomically normal children. This diagnosis depends on two modalities of investigation

1) Urodynamic Study (CMG with perineal EMG).

A Urodynamic study has two basic aims (26):

- To reproduce the patient’s symptomatic complaints during urodynamics.
- To provide a pathophysiological explanation by correlating the patient’s symptoms with the urodynamic findings.

In a case of Non Neurogenic Neurogenic bladder urodynamics not only demonstrates the disturbed bladder dynamics (elevated filling pressure, detrusor instability, high resting sphincter EMG, detrusor sphincter dyssynergia,) but also plays an important role in determining the modality of further treatment. The only drawback of this study is, findings can be fallacious in presence of a major reflux. In our study Cystometrogram was done for initial 10 patients, a technical snag prevented subsequent study.

2) Absence of posterior urethral valve, spinal lesion or syndromes.

Non Neurogenic Neurogenic bladder is a diagnosis of exclusion. Only after an anatomic bladder outlet obstruction and a spinal lesion are ruled out, does a patient with LUTS and severe upper tract dilatation qualify to be labeled as a Non Neurogenic Neurogenic bladder. Ultrasonography and Micturating cystourethrogram was done in all patients (N=28). These combined with urethra-cystoscopy (N=26) ruled out a posterior urethral valve in our patient population. Non Neurogenic Neurogenic bladder has all the clinical and urodynamic features typical of neuropathic bladder dysfunction but no neurologic pathology can be demonstrated. Ideally an MRI is a must to rule out a spinal lesion. In our study MRI was selectively done (N=3), this we believe is a weakness of this study.

Role of MRI in the diagnosis of Non Neurogenic Neurogenic Bladder

Daytime incontinence is a common paediatric problem. Most children with daytime wetting

have detrusor instability. It is important to identify the minority in whom wetting is caused by neuropathic vesicourethral dysfunction as these children are at risk of renal damage and ultimately renal failure. In addition there may be spinal cord abnormality requiring neurosurgical intervention and, although controversial, spinal cord untethering in those in whom the spinal cord is tethered may prevent further deterioration and improve long term bladder and neurological function.

Most cases of neuropathic vesicourethral dysfunction are secondary to spinal cord pathology, and magnetic resonance imaging (MRI) of the spine is the optimum imaging

technique for detecting this. However, it would be inappropriate to investigate all children with voiding dysfunction in this way. Incidentally detected failure of fusion of the fifth lumbar (L5) and first sacral (S1) vertebral arches alone should be distinguished from closed spina bifida. The former is a normal variant occurring in an estimated 10% of the population, and is not associated with an increased incidence of underlying spinal cord pathology. Indications for MRI spinal cord imaging in children with voiding dysfunction in the absence of cutaneous, neuroorthopaedic, or plain lumbosacral spine x-ray abnormalities remains controversial.

Pippe Salle in there study of patients with normal neuro-orthopedic examination and dysfunctional elimination syndrome reported that MRI should be used in patients with abnormal physical findings or complex abnormality on spinal x-ray.

KAfshar et al (13) noted that spinal MRI has a low impact on the management of LUTS. With proper case selection the pre test probability of positive MRI may be increased and therefore many unnecessary studies may be avoided.

In contrast Douglas A Canning in an editorial comment (25) and E Wraige believe spinal cord imaging by MRI should be considered in children with incontinence when this is associated with impaired bladder sensation or poor emptying even in absence of neuro-orthopedic,

cutaneous or lumbosacral spine x-ray abnormalities. They believe a detrusor instability may be the earliest sign of an occult spinal lesion.

Luis et al (24) noted, after untethering day time incontinence improved dramatically, this was confirmed urodynamically as well. But they also commented on lack of proven indication and long term follow up data of surgical intervention in occult spinal dysraphism.

We believe, MRI although a sensitive modality is overkill in absence of adequate indication. The yield is poor in absence of cutaneous and neuro-orthopedic abnormality. It is expensive and requires General Anaesthesia in young children. Our protocol is to evaluate the child with a thorough neuro-physical examination and a LS spine x-ray. MRI is done if there is a cutaneous stigmata and an underlying spina bifida. Presence of Spina Bifida Occulta doesn't change the sequence of management in a patient with severe voiding dysfunction. In a case of severe dysfunctional voiding syndrome, management of bladder to preserve upper tract deterioration takes precedence. In this study spine was evaluated clinically and with a lumbosacral plain x-ray to document an occult spina bifida. MRI was done selectively in our protocol. Three of our 28 patients who had suspicious cutaneous stigmata of spinal dysraphism underwent MRI. Two had spina bifida occult without tethered cord, while third patient had normal spine

Surgical group I

Consist of patients (N=6) with early bladder changes with major reflux. These patients mainly presented with major “primary” reflux which on investigation revealed subtle signs of “secondary” reflux. These subtle findings were bladder trabeculation, dilated posterior urethra in the absence of valve, safe bladder capacity less than calculated capacity in spite of major reflux and presence of hydroureteronephrosis of the contralateral non refluxing unit. Major reflux secondary to dysfunctional voiding does not resolve spontaneously and causes increased scarring. Reimplantation alone is dangerous and will result in deterioration of renal function. Similarly in presence of major reflux CIC may predispose to frequent pyelonephritis and resultant scarring. Adding a catheterisable channel for the purpose of CIC in addition to reimplantation is an useful adjunct in these subset of patients. Reimplantation with a mitrofanoff port was done in 5 patients while 1 with reflux underwent only reimplantation (this patient was taught urethral CIC). There were 10 refluxing units for antireflux procedure .Follow-up MCU was available in 7 renal units (5 Patients) for an average duration of 10.5 months (5mths-21mths). There was complete reflux resolution in 5 units (71%). 1 non dilated refluxing uretric orifice (managed conservatively) continued to reflux. One refluxing unit had a failed reimplant. Ultrasonographic evaluation of 10 renal units in this group at follow-up showed decreased Hydroureteronephrosis in 7 units, whereas 3 renal units were stable. None of the 6 patients had raised preoperative serum Creatinine.

Average preoperative serum Creatinine was 0.76mg% in this category, while post operative Creatinine was 0.71mg%. All the patients are compliant with intermittent catheterization. 1 patient is doing urethral CIC while rest are using their mitrofanoff port for intermittent catheterization and night drainage.

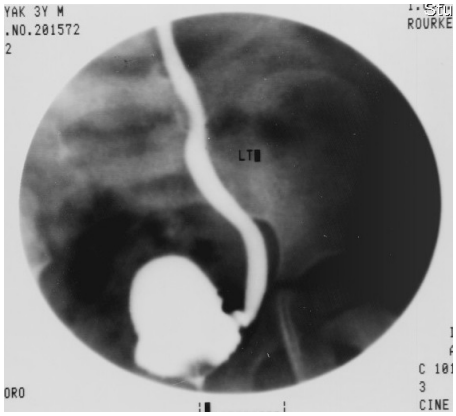
Bladder dysfunction and Vesicoureteral reflux

Dynamic changes can affect ureterotrigonal structure and result in VUR (2). The association between nonneuropathic or nonanatomical abnormalities of lower
urinary tract function and VUR in infants and children is well known. Increased intravesical pressures cause a spectrum of intravesical anatomical distortions that predispose to VUR. On the contrary in a small subset of patient gross reflux itself can predispose to bladder dysfunction by maintaining a constant preload of urine (the refluxed volume). Historically both bladder dysfunction entities, the overactive bladder (OAB) and the dysfunctional voiding (DV) have been described in conjunction with VUR. Voiding phase dysfunctions (DV and DES) (High Pressure) are considered more severe than the genuine filling phase dysfunction (OAB) (Low pressure), with an increased frequency of UTI and renal damage in the former groups (7).

Reflux in a setting of Non Neurogenic Neurogenic bladder is classified as a secondary reflux. Secondary to functional outlet obstruction, high pressure bladder and significant residual urine. These reflux tend to be of high grade and are associated with significant scarring. Because of their secondary nature it is unlikely to resolve spontaneously.

Child with recurrent UTI, MCU showed Left VUR with small bladder and mild trabeculation. Right kidney mild Hydronephrotic. Underwent Left Reimplant and Mitrofanoff for CIC.

Pre operative MCU **Nuclear scan Scan (Pre-op)**

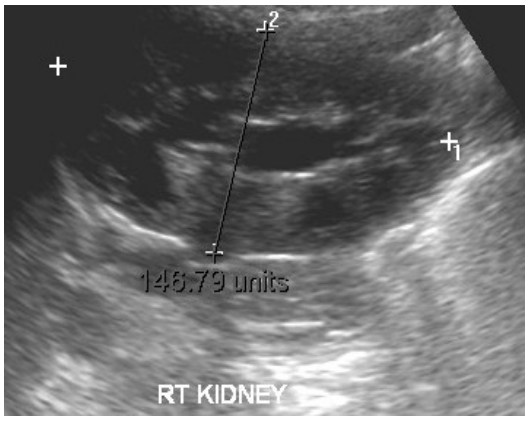


side with small capacity, Trabeculated bladder

Scarred Left kidney with 21% Function

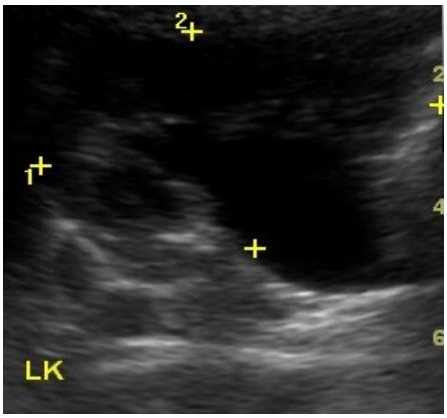
—

Contralateral Non Refluxing Renal unit



Hydroureteronephrosis of the nonrefluxing renal unit

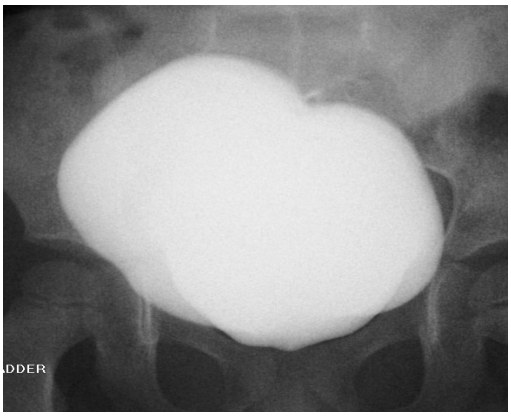
Refluxing Renal Unit

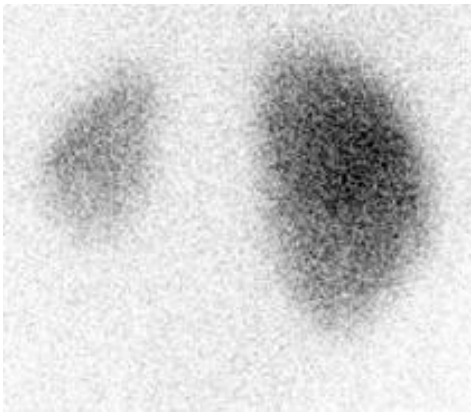


Hydroureteronephrosis of the Refluxing renal unit

Post operative MCU

Post operative Nuclear Scan



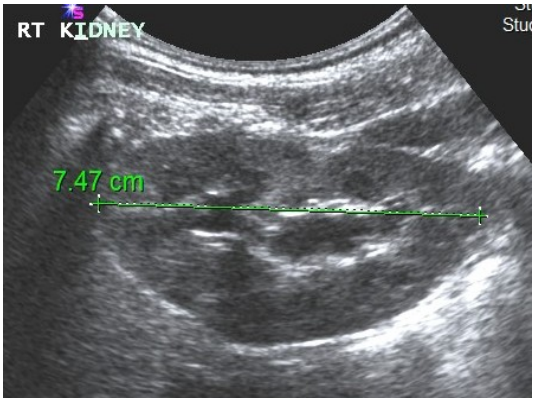


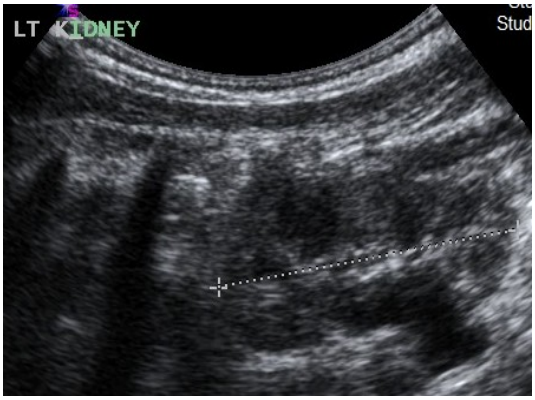
Improved capacity bladder with resolution of Reflux

No further scarring at Follow up

.

Post operative ultrasound of Kidney





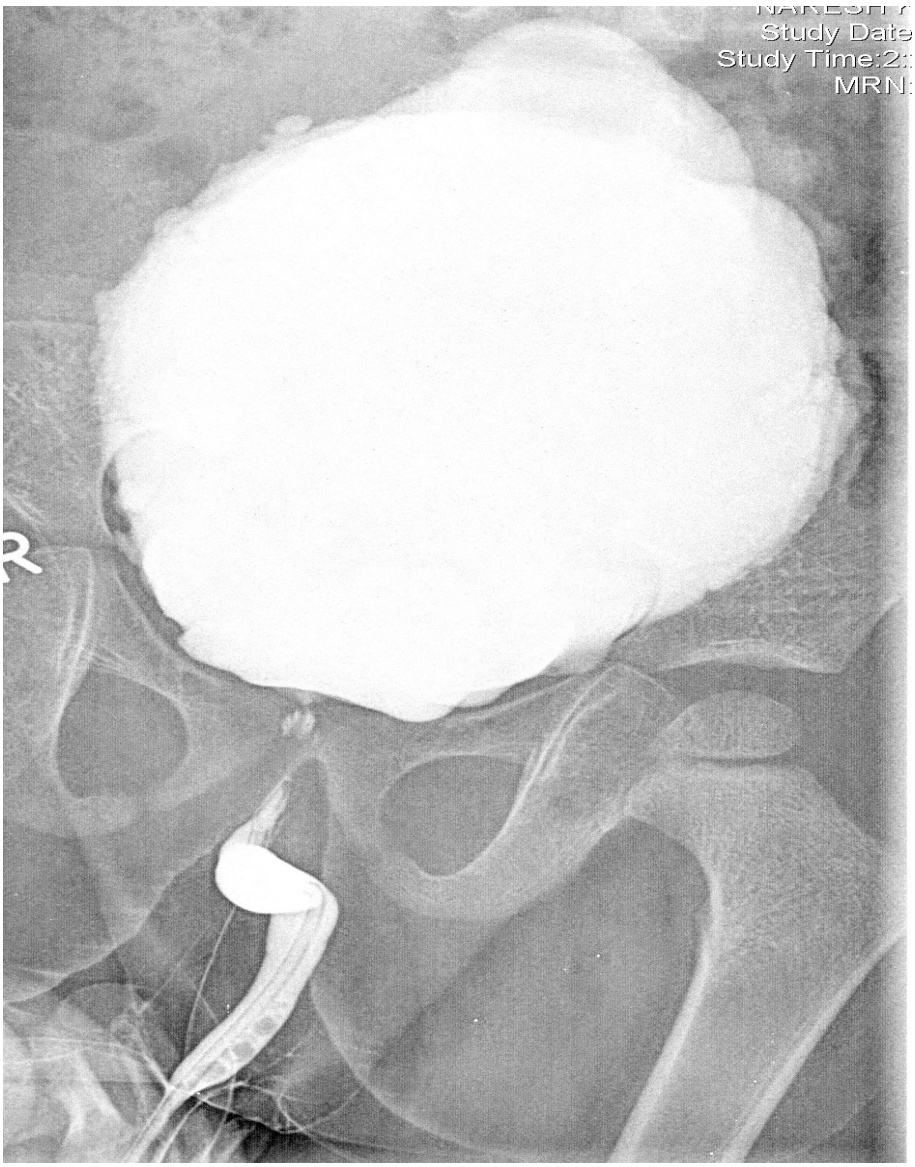
Resolution of non refluxing Hydroureteronephrosis

Resolution of refluxing Hydroureteronephrosis

Surgical group II

Consists of patients with early bladder changes without reflux (N=1). Although a natural history is only speculative this group may represent an early stage of Non Neurogenic Neurogenic bladder. Urodynamically these patients may have unstable baldder and/or cystometric safe bladder capacity close to expected bladder capacity. These patients present with minor degree of trabeculation and significant post void residue (in absence of reflux). Anticholinergics and effective bladder emptying by clean intermittent catheterization is the treatment of choice. Route of Clean intermittent catheterization is controversial. Although appendicular mitrofanoff provides a painless channel for CIC, this should be tried only if urethral catheterisation is not accepted. 1 patient presented with trabeculated bladder, dilated upper tracts (No VUR) and significant residual urine in this study. He underwent mitrofanoff procedure for CIC. At follow up after 6.5 years, he showed remarkable resolution of Hydroureteronephrosis as well as bladder trabeculation.

Pre operative Micturating Cystourethogram

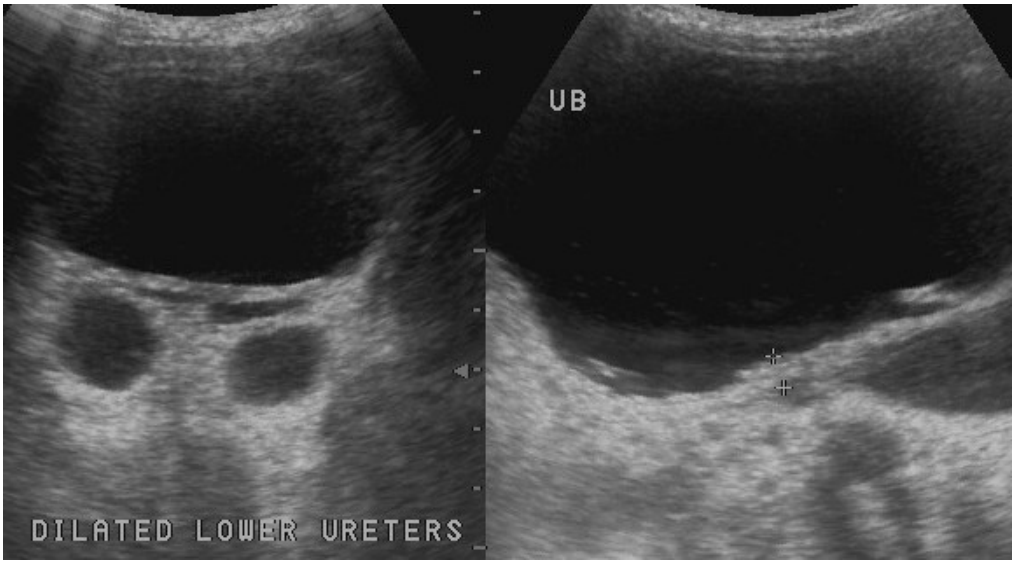


Trabeculated bladder without reflux

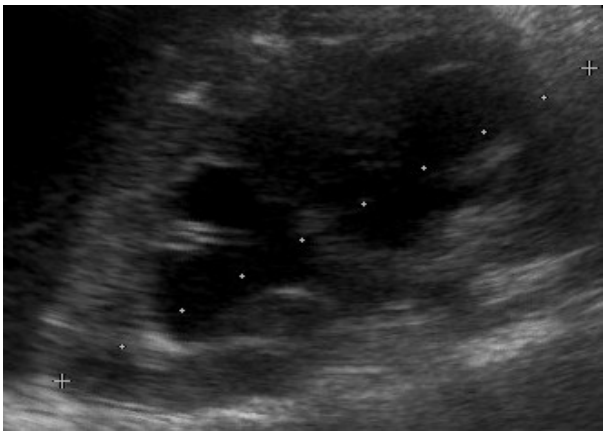
Postoperative (Mitrofanoff alone) Micturating Cystourethrogram

Resolution of trabeculation with regular CIC via Mitrofanoff

Preoperative Ultrasonography



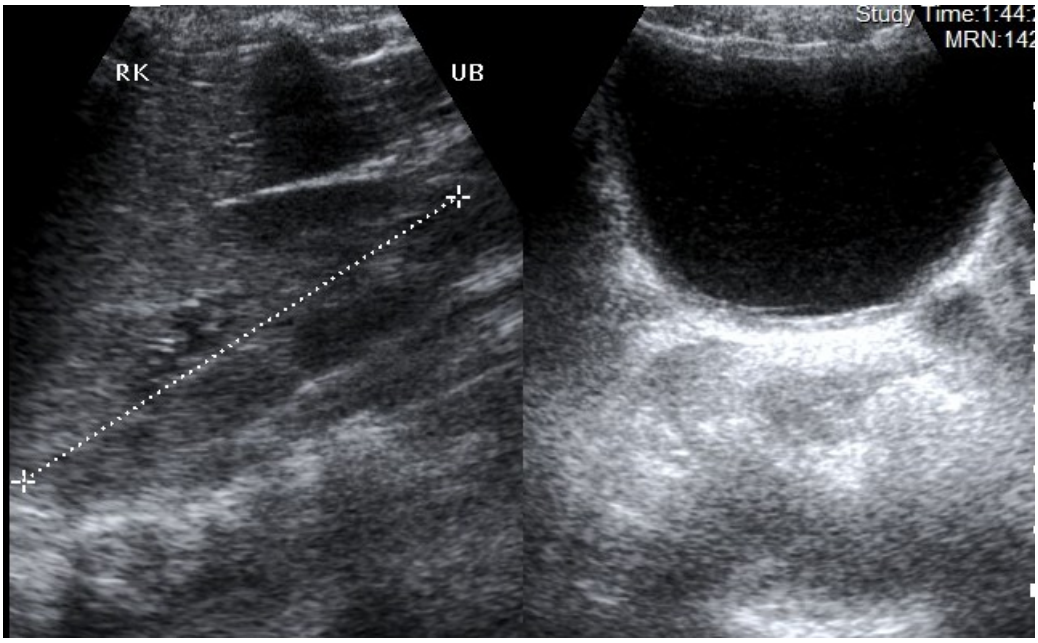
Bilateral Hydroureteronephrosis with Trabeculated bladder



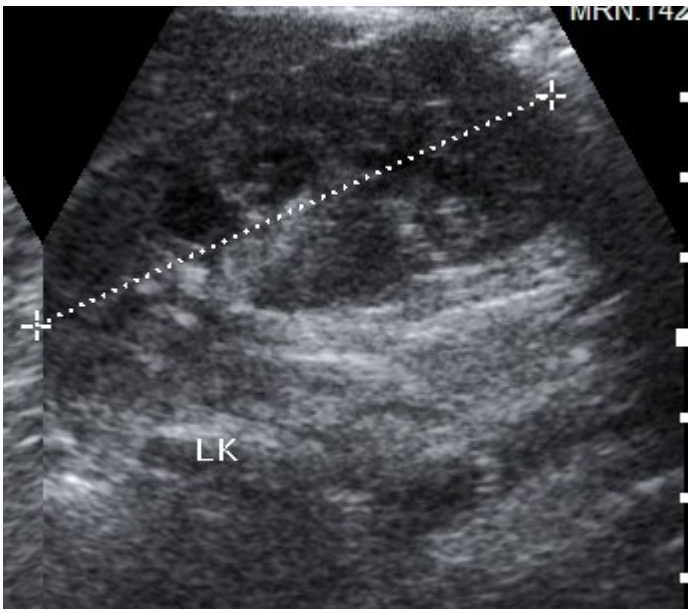
Right Hydroureteronephrosis

Left Hydroureteronephrosis.

Post operative Ultrasonography

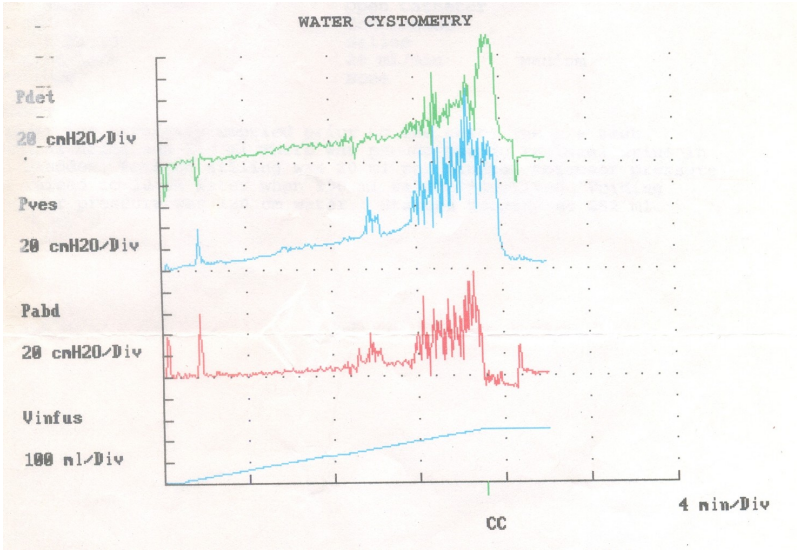


Resolution of Right Hydroureteronephrosis and Bladder Trabeculation.



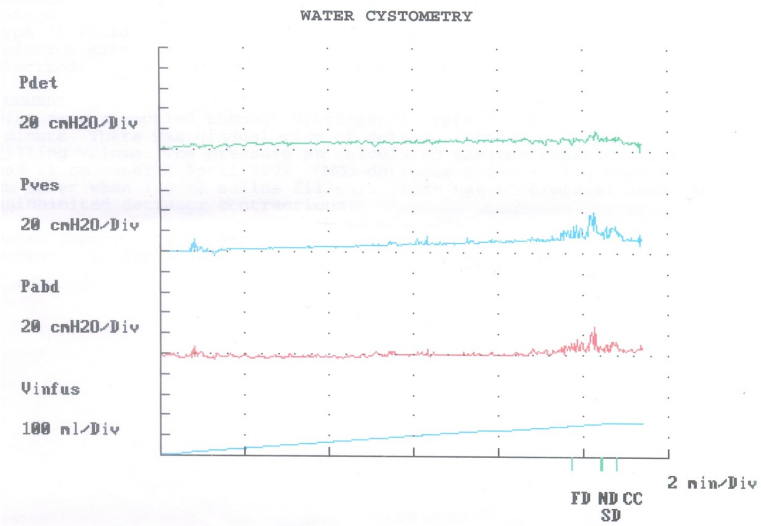
Resolution of Left Hydroureteronephrosis

Saline Cystometrogram (CMG)



Preoperative CMG

Mod compliance, without instability. Volume at 20cm H2O 136ml (90% of exp)



Postoperative CMG

Improved compliance with oxybutynin and CIC

Surgical group III

Represents patients at the severe end of the dysfunctional voiding spectrum (N=17). They have severe bladder trabeculation with more advanced Hydroureteronephrosis and reflux. A high pressure bladder due to detrusor sphincter dyssynergia has resulted in progressive decline in renal reserves and impending renal failure. Aim of the surgical intervention is to create a low pressure system which allows effective drainage of upper tracts and prevents reflux.

CIC (via mitrofanoff/urethra) is an established technique of reducing bladder pressure, but CIC alone is not safe in small capacity bladder or in presence of reflux. To be effective, bladder has to store urine at a low pressure in between CIC, so that patient or caregiver can do intermittent catheterization at convenient duration (3 or 4 hourly). In presence of reflux CIC may predispose to frequent pyelonephritis and resultant scarring. All these issues can be

addressed reliably by an Augmentation Cystoplasty with mitrofanoff port and uretric reimplantation.

Management of reflux during Augmentation

Management of a refluxing ureter during augmentation is determined by factors like nature of uretric orifices, bladder trabeculation and grade of reflux. Although an augmentation alone is sufficient for reflux resolution in a high pressure system, a dilated uretric orifice in a non compliant bladder may not always resolve with augmentation alone. Reimplantation into the native bladder is the first choice, if this

can be safely done (these severely trabeculated bladder may be a limiting factor). In case of an unilateral reflux where the contralateral ureter is dilated, a Transuretero-ureterostomy is an acceptable technique of reflux management. Reimplantation into the bowel, in the form of a nipple can be undertaken when above mentioned options are not available. A severely dilated, tortuous ureter with a non functioning kidney can be used for augmentation.

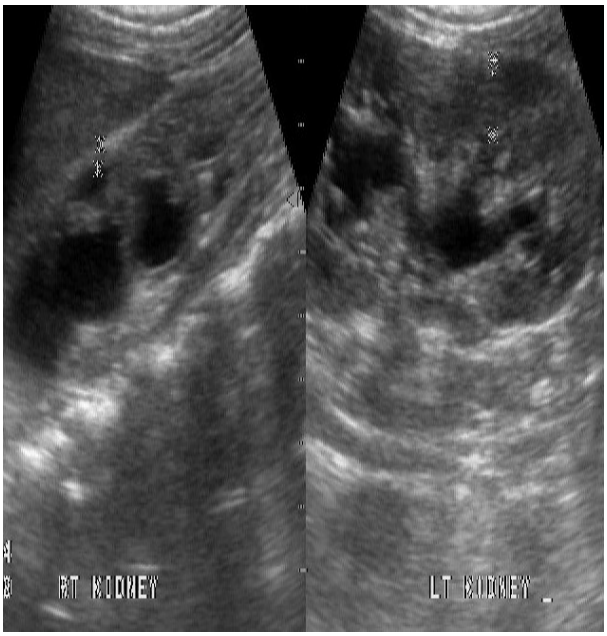
A well timed augmentation of the bladder stabilizes serum Creatinine and dilatation of upper tracts. In these 17 patients post operative Creatinine decreased to an average of 0.8mg % compared to there Pre-operative value of 0.95 mg%. Patients (N=5) with raised pre operative serum Creatinine (Average 1.6 mg %),at follow up had an average value of 0.96 mg%.

30 renal units were dilated preoperatively. At follow up 22 renal units showed significant decrease while 6 had stable Hydroureteronephrosis.

16 refluxing units were addressed in this treatment modality. A variety of antireflux techniques were used (Reimplantation into bladder, Transuretero-ureterostomy, Reimplantation into Bowel portion of the augmentation and Augmentation alone). 13 preoperative refluxing units

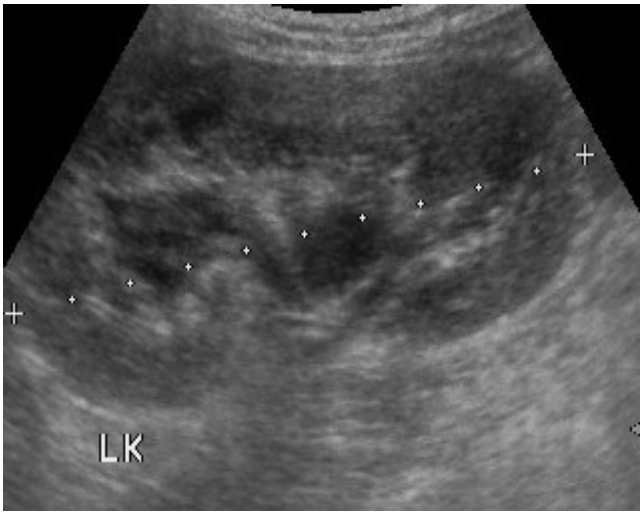
were reviewed with post op MCU. All 13 showed reflux resolution.

Pre Augmentation Ultrasound



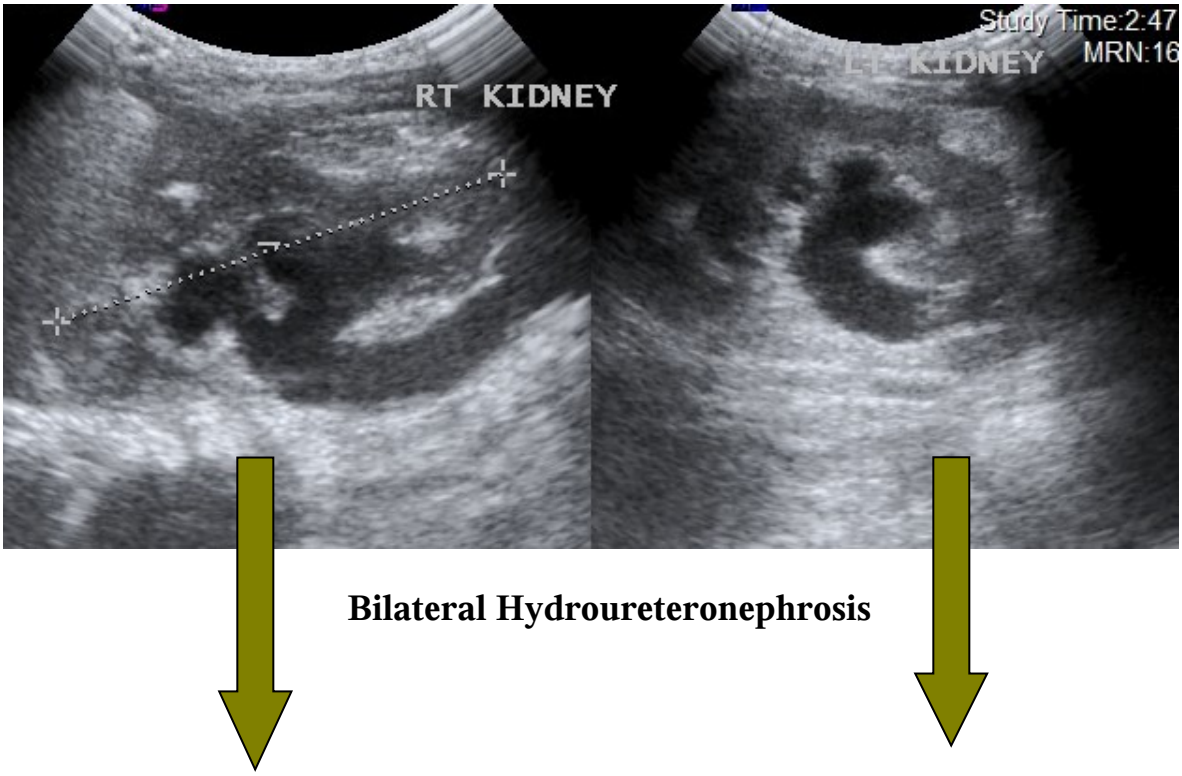
Mild Hydroureteronephrosis

Post Augmentation Ultrasound

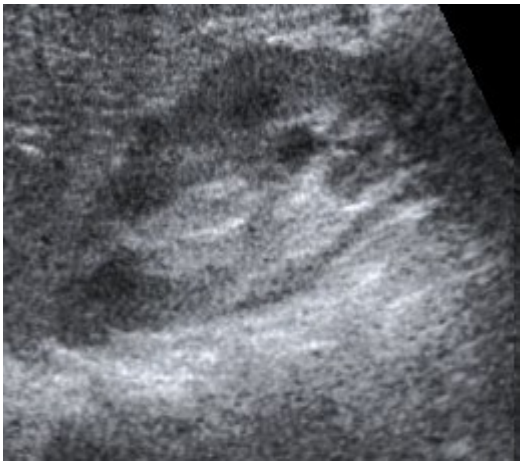


Resolution of Hydroureteronephrosis

Pre Augmentation Ultrasound



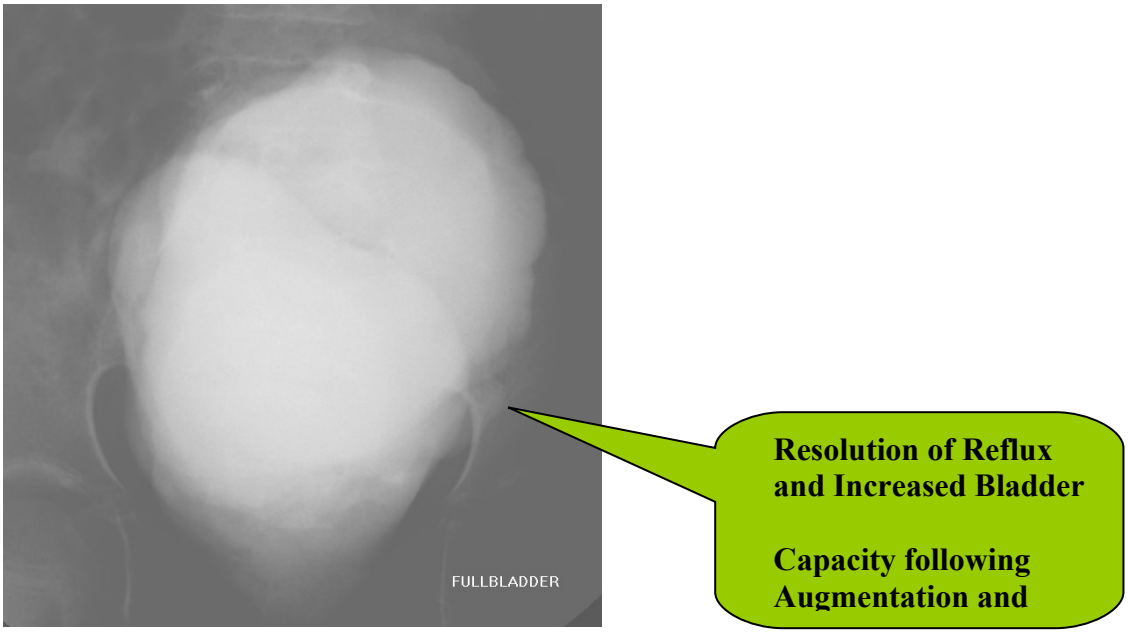
Bilateral Hydroureteronephrosis



Post Augmentation Resolution of Bilateral Hydroureteronephrosis

Pre Augmentation Micturating Cystourethogram

Post Augmentation Micturating Cystourethogram



Surgical group IV (N=4)

Consists of patients with advanced bladder changes with established renal failure.

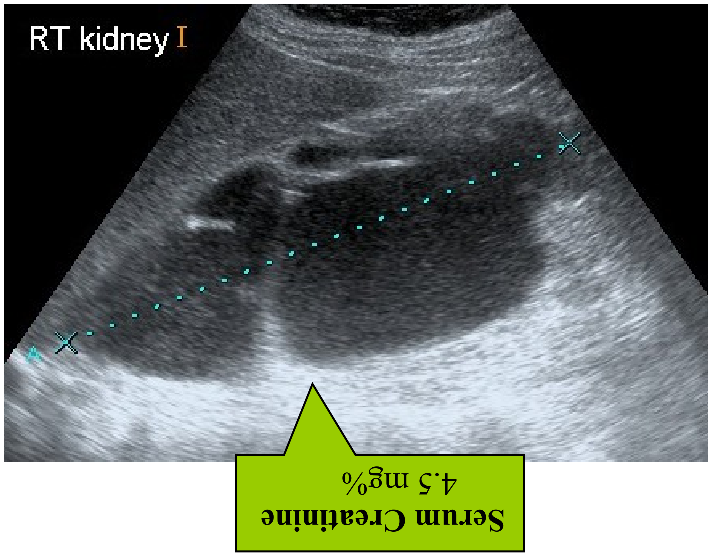
Aim of intervention is to assess reversibility of renal failure and provide drainage during urosepsis. This is achieved with a resistance free diversion like Ureterostomy (N=1), Vesicostomy (N=2) or an intestinal (Ileal) conduit (N=1).

This group also includes patients presenting at a younger age when a diversion is done to postpone a complex reconstruction.

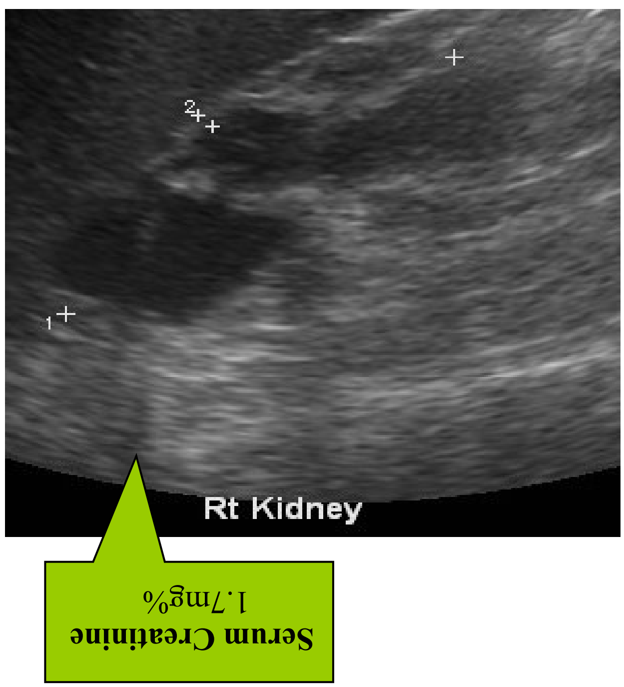
In the Vesicostomy group average Creatinine dropped from 1.45mg% to 0.5mg%

The child who underwent ileal conduit too showed significant recovery, his Creatinine decreased from 4.5 mg% to 1.7mg%.

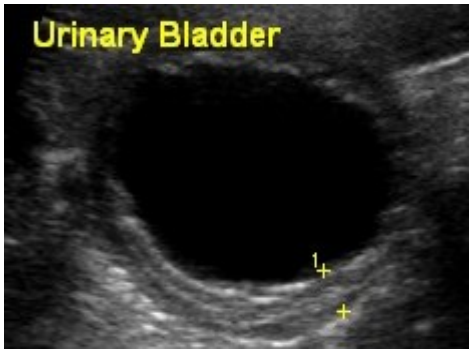
Pre Diversion UltraSonography - Intestinal Conduit

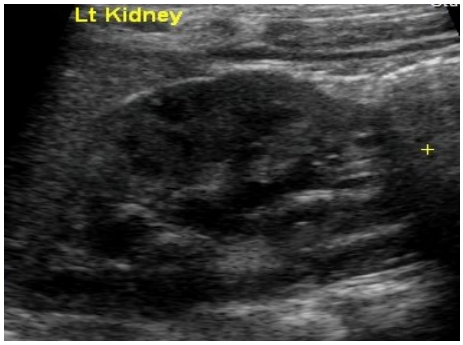


Post Diversion UltraSonography



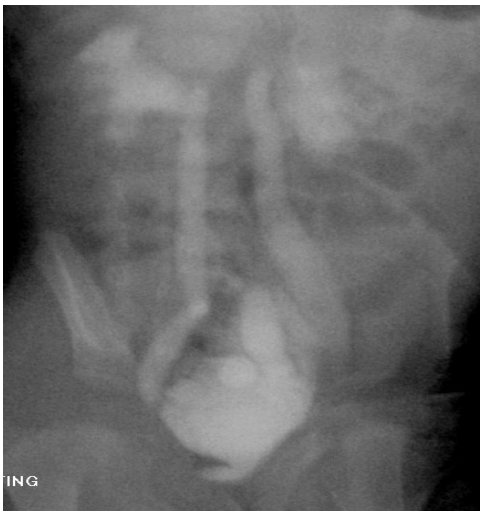
Infant: Pre-Diversion



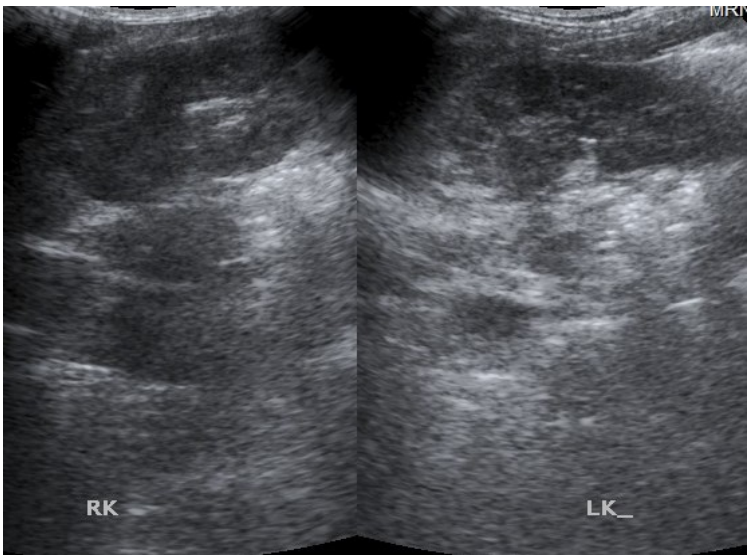


Bilateral mild Hydronephrosis with Severe Trabeculated Bladder in an Infant

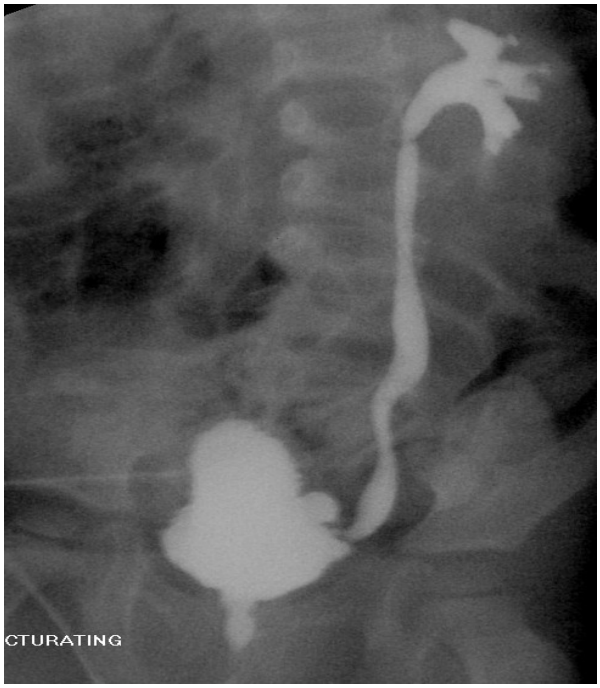
Severe Bladder Trabeculation, Bilateral Major Reflux



Post diversion “Vesicostomy”



Resolution of Hydroureteronephrosis



Resolution of unilateral VUR. Bladder remains Trabeculated.

Conclusion

- Dysfunctional voiding syndrome has a spectrum of presentation. Majority of the children with this disorder are treated medically. Non Neurogenic Neurogenic bladder represents a severe form of dysfunctional voiding characterized by upper tract dilatation and renal damage. This rare subset of patient requires surgical intervention to protect the upper tract and achieve continence. 28 such patients were identified in the last 10 years and formed the basis of this study.

- Aim of surgery is to provide a low pressure reservoir which can be evacuated effectively. Surgical procedure should be individualized and guided by bladder quality, presence of reflux and renal function. Surgical procedures are classified into four groups
  1) Reimplantation for major dilating VUR with a continent catheterisable channel (N=6) for bladder management.
  2) Continent catheterisable channel alone (N=1) as bladder management.
  3) Augmentation Cystoplasty with or without antireflux procedure & a Continent catheterisable channel (N=17).
  4) Incontinent diversion (N=4).

- Diagnosis of dysfunctional voiding in a patient with reflux requires high index of suspicion. Some clues to an underlying detrusor sphincter dyssynergia are
  1) Bladder trabeculation in the absence of Neurogenic cause or a PUV,
  2) Dilatation of the contralateral upper tract in a unilateral reflux.

3) Dilatation of posterior urethra secondary to external sphincter spasm.

4) Poor compliance on CMG in spite of gross reflux.

- Refluxes in the setting of NNNB are major dialating types with evidence of renal scarring (out of 32 refluxing units in the study only 1 was a minor grade 1 reflux). Hence Reflux management forms an important component of treatment protocol. Outcome of reflux management is best when an antireflux procedure is combined with bladder augmentation and mitrofanoff (100%) vs reimplantation with mitrofanoff (71%) but without augmentation. However, augmentation was done only when advanced bladder changes were present.
- With planned surgical management and CIC, renal damage is partially reversible.
- Diversion could be a temporizing procedure in a young child or definitive treatment in older children with more advanced renal failure.

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Appendix

NONNEUROGENIC NEUROGENIC BLADDER SYNDROME

1. NAME: AGE AT PRST'ION/SEX :
2. HOSPITAL NO:
3. ADDRESS/PHONE:

PRESENTING COMPLAINS/ INCONTINENCE QUESTIONNAIRE:

4. EXAMINATION:

MOTOR:

BULK: SIZE
SHAPE
SYMMETRY

TONE:

MOTOR

POWER:

Lt 0 1 2 3 4 5

Rt 0 1 2 3 4 5

REFLEX:

SUPERFICIAL: ABDOMINAL

CREMASTERIC

ANAL

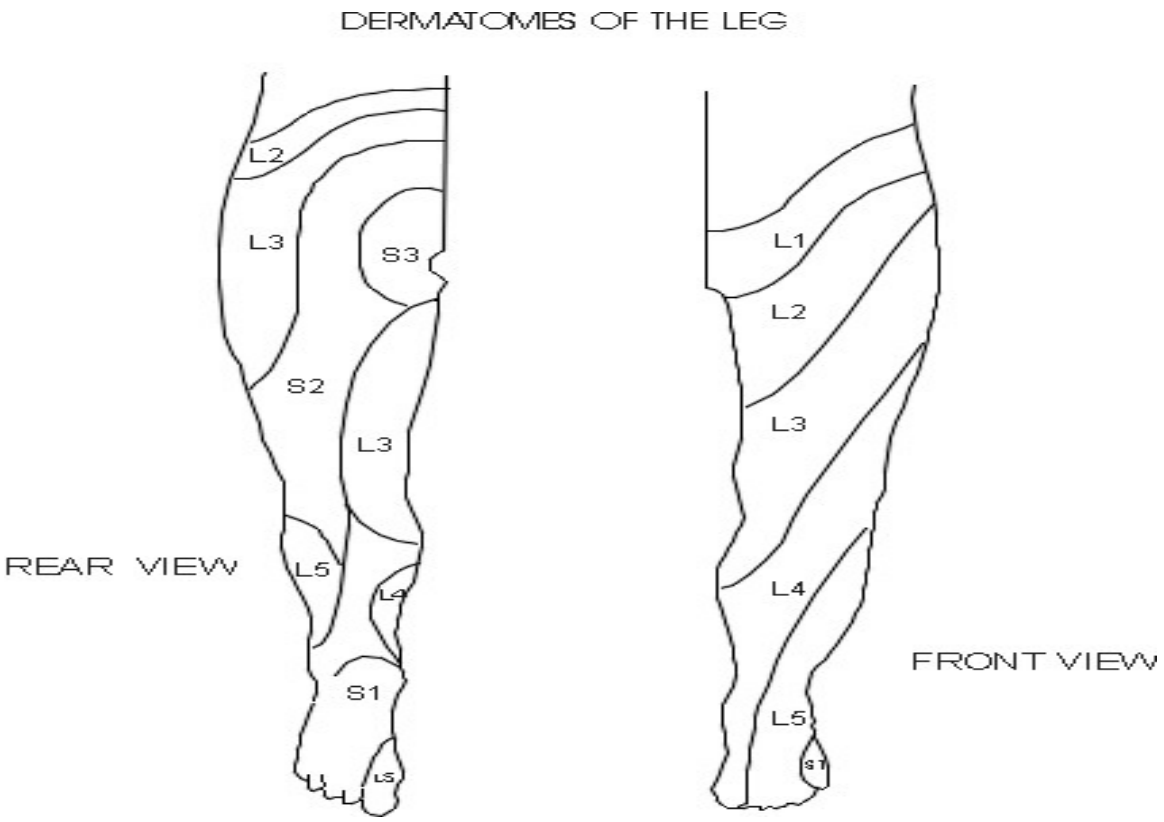
PLANTAR Rt Lt

DEEP : RT LT

KNEE:

ANKLE:

SENSORY



SPINE

GAIT

INVESTIGATION:

- ULTRASOUND:

KIDNEY

URETER

BLADDER

- BIOCHEMISTRY

  CREATININE

  ALK PO4

  HCO3

- URINE CULTURE(COLONY COUNT):

- SPINE XRAY(AP/LAT):

- CT/MRI

INVESTIGATION:

- MCU

- CMG

Treatment

- Initial

- Follow-up

- Surgery

- Follow-up

Mastercharts